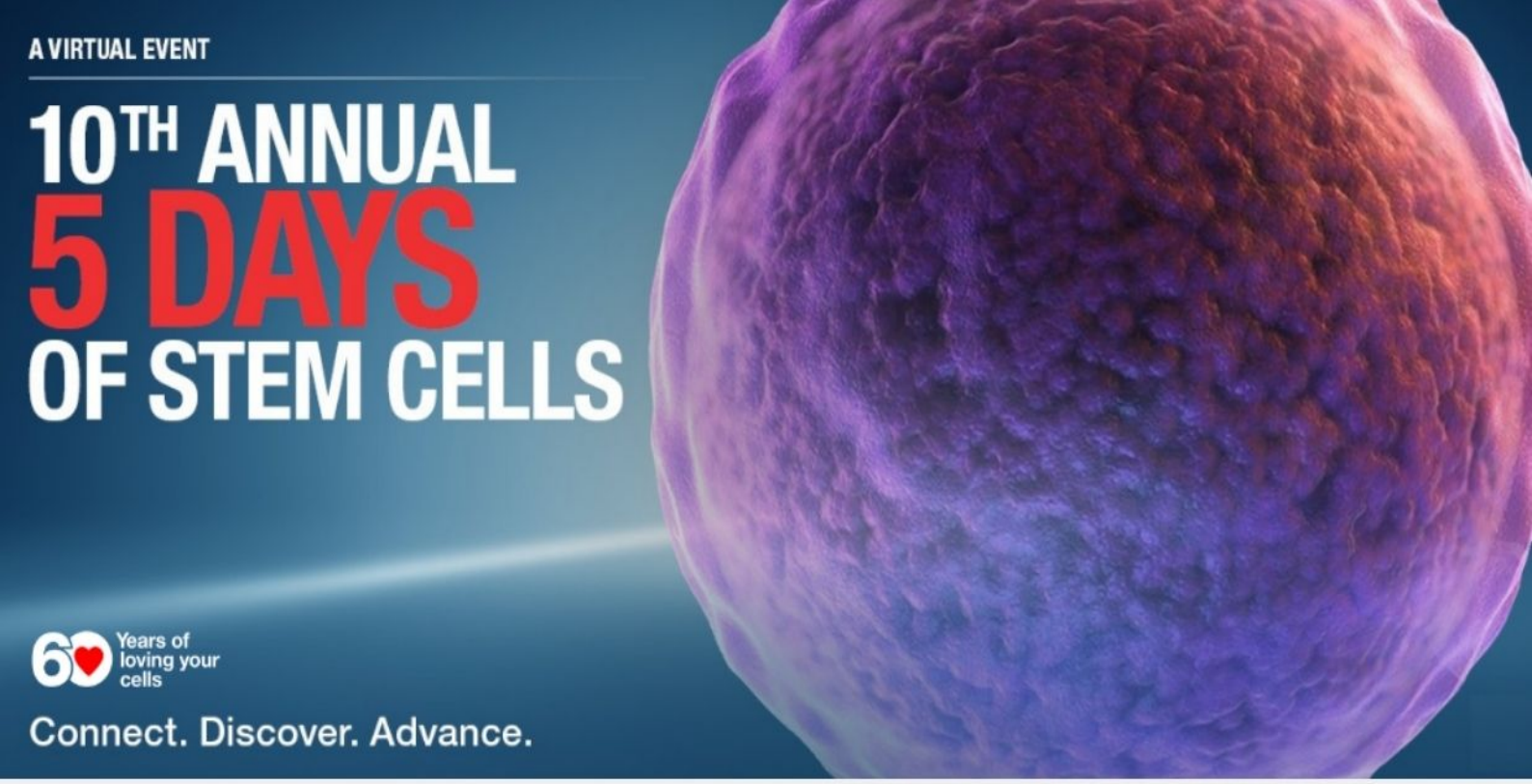

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Micheletti Serena (Orcid ID: 0000-0003-2313-5824)
GALLI Jessica (Orcid ID: 0000-0002-3347-7548)

VISUAL INTERVENTION IN EARLY ONSET VISUAL IMPAIRMENT: A REVIEW

Running title: Early visual intervention: a review

Micheletti Serena[1], Merabet Lotfi B.[2], Galli Jessica[1,3], Fazzi Elisa[1,3]

[1] ASST Spedali Civili of Brescia, Unit of Child Neurology and Psychiatry, Brescia, Italy

[2] The Laboratory for Visual Neuroplasticity, Department of Ophthalmology, Massachusetts Eye and Ear, Harvard Medical School, Boston, MA, USA.

[3] Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

Micheletti Serena
ASST Spedali Civili of Brescia, Unit of Child Neurology and Psychiatry, Brescia, Italy
serena.micheletti@unibs.it
ORCID: 0000-0003-2313-5824

Merabet Lotfi B.
The Laboratory for Visual Neuroplasticity, Department of Ophthalmology, Massachusetts Eye and Ear, Harvard Medical School, Boston, MA, USA.
lotfi_merabet@meei.harvard.edu
ORCID: 0000-0002-8094-9536

Galli Jessica
Department of Clinical and Experimental Sciences, University of Brescia, Brescia; ASST Spedali Civili of Brescia, Unit of Child Neurology and Psychiatry, Brescia; Italy
jessica.galli@unibs.it
ORCID: 0000-0002-3347-7548

Fazzi Elisa
Unit of Child Neurology and Psychiatry, ASST Spedali Civili of Brescia; Italy; Department of Clinical and Experimental Sciences, University of Brescia, Brescia; Italy
elisa.fazzi@unibs.it
ORCID: 0000-0003-4805-7906

Correspondence author:
Serena Micheletti
ASST Spedali Civili of Brescia, Unit of Child Neurology and Psychiatry, Brescia
Piazzale Spedali Civili 1 25123
Brescia, Italy
Tel. 00390303995724
Fax.00390303995726
email: serena.micheletti@unibs.it

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ABSTRACT

Vision is a primary and motivating sense. Early visual experience derived from the external world is known to have an important impact on the development of central visual pathways and, not surprisingly, visual impairment constitutes a risk factor for overall development. In light of the role of vision in early brain development, infants and young children with visual impairment should be thus entitled to early and effective visual intervention programs. In this review, we discuss early visual interventions in infants and young children with visual impairment, focusing on their contents and outcomes. We defined a PICO format to critically review different models with a particular focus on parent-mediated and therapist-mediated approaches. We consider protocols that involved direct manipulation or improvement of the infants' visual inputs or were based on behavioral strategies and communication towards infants with visual impairment. We also provide an overview of the effectiveness of these protocols. A total of nine intervention protocols were selected for the purposes of this review. Substantial agreement regarding the importance of promoting the enrichment of infant environments, and more specifically in the context of active play that engages the whole family, has been reported in most of the studies. However, there is no clear agreement on methodological aspects, including clinical population characteristics, outcome measures, length of treatment, and follow-up programs. Further high-quality, carefully designed and adequately reported studies are needed in order to improve the clinical efficacy of these approaches to treating infants with visual impairment.

INTRODUCTION

Visual impairment (VI) has been defined as an impairment of visual capacity, in terms of visual responses to light and structured stimuli, caused by congenital or acquired pathologies of the eye and/or of the central visual pathways (Dale et al. 2017). VI can concern all pre-geniculate ophthalmological disorders of the ocular globe up to the optic chiasm (peripheral visual impairment – PVI), or be caused by damage to or malfunction of post-geniculate visual pathways (cerebral visual impairment – CVI). VI could be identifiable in the early months of life (Ricci D et al 2008, Rossi A et al 2017), persists throughout an individual's lifetime (Galli J et al 2022a), and is likely to have an impact on all areas of development (Dutton & Jacobson 2001; Fazzi et al. 2002; Good et al. 2001; Sakki et al. 2018), namely the organization of the sleep–wake rhythm (Fazzi et al. 2008), motor skills (gross motor and fine motor, Fazzi et al. 2002), spatial awareness (Iossifova & Marmolejo-Ramos 2013), cognitive functions (Bedny & Saxe 2012; Pring & Tadić 2010), communication and language (Bigelow 2003; Urqueta Alfaro et al. 2018), and maternal (Paul et al. 2019) and social relationships (Troster & Brambring 1992). Delayed acquisition of symbolic play, as well as of social and communicative skills, may also be observed and, without appropriate input, these delays may persist to become long-term developmental and behavioral problems (Pring & Tadić 2010).

Early visual experience influences the structure, the functioning and the maturation of the visual brain (Purpura & Tinelli 2020) and influences overall infant development. Since the early visual experience acts as a potential neuro-restorative factor in infants with VI (Volpe 2019), the use of visual abilities should be encouraged from the first months of life, during which the infant benefits from the greatest degree of experience-dependent neural plasticity (Chorna et al. 2020), at a different degrees according to the type of VI (Martin et al. 2016). Clinical and experimental findings (Castelli et al. 2016, Cioni et al. 2016, Chorna et al. 2020,

Fazzi et al. 2021) have indicated that for early intervention (EI) to be maximally effective, it needs to promote the modification of the natural environment through the enrichment of sensory and social experiences. EI should also entail active engagement on the part of the parents, who play the role of fundamental mediator in early mutual relationships, providing experience opportunities and goal-directed activities. Early exposure to enriched experiences, combined with active social interactions have been studied through the paradigm of the enriched environment (EE), which has shown to profoundly affect the central nervous system at the functional, anatomical, and molecular levels (Ismail et al. 2017). Much of this evidence derives from experimental studies on animal models. The first protocols that applied the paradigm of EE in mice and rats documented that being born in wide and attractive cages with a variety of stimulating objects was related to an increase in cortical thickness, in spine density and in dendritic tree complexity, as well as effects on neuromodulators such as acetylcholine and noradrenaline. These modifications enabled an improvement in the mice's learning and memory performances (Berardi et al. 2015). The exposure to an EE has also been described as being associated with an improvement in visual acuity development, as a consequence of an acceleration of factors involved in V1 cortex development (Consorti et al. 2019). Despite these promising data in animal models, less in known about the effectiveness of EE paradigm on infants' neurodevelopment. The principles of EE have been to some degree focused on the implementation of early visual intervention programs for infants with neurodevelopmental disorders.

In the case of infants with VI, there has been very limited investigation into the effectiveness of early intervention programs, in contrast to studies on other conditions such as Autism Spectrum (Sandbank et al. 2020), Attention Deficit Hyperactivity Disorder (Catalá-López et al. 2017) and Language Disorders (Rinaldi et al. 2021). This limitation could be related to the fact

that the term “Visual Impairment” constitutes a broad label including a very wide range of ophthalmic, orthoptic and cerebrally-mediated visual disorders. Therefore, the intervention strategies for treating infants affected by VI could be extremely different according not only to the presence of PVI or CVI, but also to the etiology of VI; from surgery in the case of congenital cataract (Lenhart PD et al. 2022) to visual training and environmental adaptation in the case of retinopathy and CVI (Fazzi E et al. 2021). Little is known about the optimal time, type and duration of early visual interventions, which are still poorly recommended by previous systematic reviews published on this topic (Chorna et al. 2017; Elsman et al. 2019; Williams et al. 2014). Previous discussions appear limited in scope, such as for patients with VI due to cerebral palsy (Chorna et al. 2017), or only addressed clinical populations with a broader range of neurodevelopmental disorders (Williams et al. 2014), or did not address visual function in the context of rehabilitation (Elsman et al. 2019).

Long before the recent experimental support provided by neuroscience, the first clinical conceptualization of the modern approach to early visual intervention originated about fifty years ago in the field of special education. In the mid-60s, Natalie Barraga (1965) led the way to the current concept of visual rehabilitation (Moore 1972), superseding the prevailing view of ‘‘sight-saving’’ strategies and encouraging an effective use of any remaining residual vision. In the 90s, Hyvärinen (1995) highlighted the importance of a comprehensive evaluation of the visual function and functional aspects of vision conducted by a multidisciplinary team sharing a common agreed-upon vocabulary. The concept of observing the "whole child" during the assessment of vision has been highlighted by Alimovic (1995) who assimilated the importance of evaluating both visual function and functional vision during the care of infants and children with VI, with the former describing how well the eyes and basic visual system can detect a

target stimulus, and the latter referring to how well an individual performs while interacting with the visual environment (Bennett et al. 2019).

Further relevant concepts with respect to visual intervention programs have been pointed out by Vervloed and colleagues (2006), who emphasized the distinction between visual stimulation interventions and visual training interventions. Visual stimulation consists of exposure to strong visual stimuli (such as flashing lights and brightly colored materials) to improve the development of the visual system by enhancing and changing its anatomy and physiology. Although still applied to children who show minimal responses to normal visual impressions (Tsai et al. 2016), visual stimulation is not directly linked to the behavior of the child, and can be considered too far removed from everyday ecological situations. Visual training can be considered a more ecologically valid and individualized approach program, aimed at helping children to make functional use of their sense of sight. However, the transition of these concepts from principles to clinical practice has impacted the clinical trial requirements and efforts in terms of cost and time required to complete the process (Chorna et al. 2020).

In this review, we seek to provide a comprehensive overview regarding the contents and the effectiveness of EI for promoting different aspects related to vision, in infants and young children with VI or at risk of VI aged between 0 and 5 years. We critically evaluate intervention protocols proposing visual training that directly manipulates and improves infants' visual inputs, or indirectly promotes behavioral communication strategies in the context of VI, through parent-mediated or therapist-mediated approaches. We also review the effectiveness of these intervention studies, particularly focusing on visual function and functional vision outcomes.

METHODS

Search strategy

In order to analyze the current evidence on the characteristics of EI protocols and their effectiveness in promoting visual functions in infants and children with VI, we defined a PICO (Population, Intervention, Comparator, Outcome) format to structure the literature search, which was conducted on relevant databases [Pubmed (MEDLINE) and Google Scholar]. The searches were performed between October 2019 and October 2021.

Our population of interest comprised infants and young children aged 0-5 years with a clinical diagnosis of VI, of peripheral and central origin, or at risk of VI. We considered any intervention protocol that directly manipulates and improves infants' visual inputs, or indirectly promotes behavioral and communicative strategies in the context of VI. We included studies with a placebo or alternative treatment as comparator.

Our outcome of interest primarily comprised measures of visual function and functional vision. We also reported measures on the general domains of neurodevelopment, where available.

The studies were assessed by two independent reviewers (SM and JG).

The search strategy used the following Medical Subheading (MeSH) and keyword in Pubmed (MEDLINE) including synonyms and closely related words: (("Children") OR "Infant") AND ("Vision Disorders/prevention and control"[Majr] OR "Vision Disorders/rehabilitation"[Majr] OR "Vision Disorders/therapy"[Majr]). The same search was conducted in Google Scholar ("vision/visual" AND ("intervention" OR "treatment" OR "rehabilitation" OR "promotion) AND ("children" OR "infant")).

After eliminating duplicate studies, the search results based on title and abstract were reviewed by two reviewers (SM and JG). The full texts of the articles were then assessed for eligibility (Figure 1).

Study criteria

Studies were included if they satisfied the following inclusion criteria:

- The study described longitudinal research with a placebo or alternative treatment as comparator (comparison studies, randomized control studies-RCT);

- The subjects were infants and young children aged 0-5 years;

- The subjects had a clinical diagnosis of VI, of peripheral or central origin, or were at risk of VI;

- The study detailed the outcome measures and intervention procedures;

- The visual training interventions were provided by medical providers, licensed therapists/professionals, or caregivers/parents trained by therapists/professionals;

- The articles were published in English;

Studies published in grey literature or describing surgical and pharmacological interventions or interventions based on visual stimulation were excluded.

Data extraction and quality appraisal

The following characteristics were extracted from the included studies: 1) year of publication; 2) study design; 3) participant characteristics at the baseline (i.e., sample size, mean age, age range); 4) type and severity of VI; 5) description of outcome measures; 6) duration of follow-up, and setting; 7) description of the intervention protocol both for the clinical and comparison group; and 8) duration and frequency of the intervention protocol.

As concerns the design and contents of the selected intervention protocols we followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist to

report in the text on the quality of the studies, with particular regard to the presence of bias in participant selection (type of participants' allocation, risk of attrition), in outcome measurement (on visual functions/functional vision/other developmental outcomes; measured before and/or after the treatment), in the intervention procedures (presence of a detailed description of the protocol, proposal in the first months of life, level of intensity, duration of the protocol, contents of placebo/ comparison intervention).

RESULTS

A total of 3686 articles were found in the initial search, based on titles that matched the inclusion criteria. Other articles were identified through searches in reference lists of previously retrieved reviews (13). Following the elimination of duplicates and a review of the publication title and abstract, 39 records were identified for initial consideration. Following full text examination of the 39 records, 9 intervention protocols published in the last 30 years (1991 – 2021) were selected for the purposes of this review. The design of the 9 articles varied, ranging from randomized controlled trials to comparison studies.

In the following sections, we describe visual training protocols only, given their ecologically valid and individualized approach to the promotion of the functional use of the sense of sight. The interventions, mainly directed by therapists, or by parents through the supervision of therapists, will be discussed in chronological order of publication (Table 1 and Table 2).

Evidence from the 1990s

Based on the hypothesis that active environmental interest is essential for visual development, Sonksen and colleagues (1991) conducted a comparison study to evaluate the effectiveness of a parent-mediated Program for Visual Development (PVD) in 58 infants (aged 1 to 13 months old) with either CVI or PVI (ocular malformation, retinal dystrophy, oculo-cutaneous albinism, optic hypoplasia/atrophy, cataracts, and abnormal retinal development

associated with Norrie disease). Thirty-five families were recruited in the clinical sample and 23 families acted as controls. Outcome measures included general development (evaluated by Reynell-Zinkin Scales, 1978), functional vision (qualitative assessment of visual awareness) and visual function (defined by non-parametric scales that measured aspects of spatial resolution related to acuity, visual following and tracking behavior, convergence control and sphere of visual attention for animate and inanimate stimuli) and were recorded at baseline and at 4, 8, 12 months following the PVD. In contrast to the Programme for General Development (PGD) previously published by the same author (Sonksen et al. 1984) and aimed at promoting many aspects of general development through exercises incorporated into daily play and handling routines, the PVD consisted of 6 sections of activities specifically targeting the promotion of visual functions. Parents were invited to engage their infants in their own scheduled program several times a day. At the end of the study, a consistent difference in visual progress was observed between the treated (PVD plus PGD) and comparison (PGD) groups. At 4, 8, and 12 months following the programs, the treated children achieved considerably higher median scores than the controls on all the nine scales, reaching a significant difference in the “near acuity” and “distance acuity” scales and the “following horizontal” and “following vertical” scales. Initial visual level, developmental status, and the type of VI at baseline were important determinants of visual progress within each of the nine scales. This study provided a detailed description of the intervention program in which visual activities were flexible, but yet within a general structured framework. Both overall developmental and visual outcome measures were provided and variables influencing visual progress were also detailed. The high data attrition (all four assessments were achieved for 34 out of 58 of the babies) and the mixture of both retrospective and prospective study design penalized the methodological structure of this protocol and may have contributed to results

of this study being statistically underpowered. This protocol was provided in the early months of life, and comprised goal-directed activities incorporated into daily play and mediated by parents. However, given that home visits by therapists were not reported and the established evaluation of the protocol was set at every 4 months, it appears that there was no possibility of monitoring the degree of parental support throughout the study.

In 1993, Behl and colleagues conducted an RCT on the Reach Out and Teach Curriculum (RTC) with the goal of defining the effectiveness of parent-mediated EI in infants and young children (2 to 30 months) with moderate to severe VI (binocular visual acuity between 20/200 and 20/2400, no data on the causes of VI were reported) and with no other major developmental disabilities. Eighteen infants received a weekly 1-hour "high intensity" home-based EI, while 17 infants were given "low-intensity" treatment through parent group meetings once a month. At pretest and at 1, 2, and 3 years after the pretest, infants underwent an evaluation of Motor, Adaptive, Cognitive, Personal-Social, and Communication skills by the Battelle Developmental Inventory, and parents were asked to complete self-report questionnaires about their child's health, their level of stress and functioning, and the occurrence of dramatic events in the family. No outcome measures on visual function or functional vision were reported. The "high intensity" program consisted of a curriculum of activities for infants with disabilities, supplemented with strategies addressing visual impairments from the Reach Out and Teach Curriculum (Ferrell, 1986)). Familiar toys and household items were used as treatment tools in the scheduled daily routines and activities. Direct services were provided once a week by certified teachers for children with VI or special needs, who were also consulted by the school teacher and/or parents, or provided direct services at home, especially during the first year. During the second and third years, experts in the field of VI from other programs provided consultation as necessary. Parents of children

in the low-intensity group (comparison group) were invited to group meetings held approximately 12 times per year for an average duration of 20.1 months. At these meetings, invited experts discussed the effects of VI on developmental areas and general activities to promote visual functions were suggested. In both groups, mixed positive and negative effects were reported on child functioning in all the annual assessments conducted for the following 3 years. No statistically significant differences were found between groups on any of the family measures. This protocol was provided in the early months of life of infants with VI, provided a modification of infants' family environment with a particular attention on the parents' involvement, even if no specific description of the type of visual-specific activities was detailed. Moreover, despite the quality of the research design, characterized by randomized assignment, the use of masked assessors, and the long-term monitoring of treatment application, the study failed to include any outcome measures regarding visual aspects.

In the comparison study by Beelmann & Brambring (1998), 10 congenitally blind infants (aged 9.5 to 19 months; 5 born at preterm, and 5 born at term, no brain damage reported) were the subject of a home-based EI twice a week across a 2 year period. A comparison group of 40 visually impaired infants aged 12-36 months without brain damage was the subject of other forms of home-based intervention, not detailed in the text. The causes of blindness included retinopathy of prematurity, optic atrophy, retinoblastoma, retinal dysplasia, Leber's congenital amaurosis, microphthalmia, glaucoma and anophthalmia. Outcome measures evaluated at 12, 15, 18, 24, 30 and 36 months assessed functional vision and consisted of the Bielefeld Developmental Test for Blind Infants and Preschoolers (BEB-KV), which involves six scales assessing general development (neuromotor skills, cognition, language, socioemotional development) and blindness-specific development

(orientation and mobility, fine-motor and daily living skills). A team of qualified psychologists, a special needs teacher and an orientation and mobility instructor all participated in the training of infants through a rehabilitation program focused on specific aspects of VI, including tactile and auditory object perception, spatial orientation and mobility and daily living skills. Parents were given guidance and training on parent–child interaction. The average duration of EI was 24.0 months with an average of 33.4 sessions across all 10 project families. The mean duration of sessions was 182 minutes. In the infants and young children born full-term, the intervention group showed significantly higher scores than the comparison group on general development scales at 30 months (large effect size), but not at any of the other time points. In preterm children, differences between the intervention and comparison group tended to be small. This study provided detailed and useful suggestions in terms of the design of EI for blind infants and their families, despite the lack of significant positive effects of the intervention in the clinical group. Particular attention was paid to the parents, who accompanied and interacted with their infant activities. This program also involved instruction and the implementation of various forms of environmental enrichment. Methodological issues with this study included the non-homogeneous selection of participants at baseline in terms of severity and causes of VI. Moreover, the outcome measures were related only to functional vision with the absence of measures of visual functions.

New Evidence

The previous studies came around 20 years before the more recently available EI protocols for infants and young children with VI or at risk of a visual disorder.

Unlike what has been described so far, the following RCT was offered to infants who, given their premature birth, were at risk of developing a VI. Sgandurra and colleagues' RCT (Sgandurra et al. 2017) investigated the short-term effects of CareToy training on motor and

visual development in preterm infants. Data was initially collected from a pilot study on 20 infants (Sgandurra et al. 2016). Forty-one preterm infants (gestational age: 28+0 - 32+6; age: 3.0± 5.9 months of corrected age) with no severe neurological and sensorial deficit (with no severe or profound VI among them) were enrolled and randomized into two groups: CareToy (19 infants) and Standard Care (22 infants). All infants were assessed before the intervention phase (T0), at 4 weeks post-treatment (T1) and 4 weeks after the reallocation treatment (T2). Data on T3 (at 18 months of corrected age) have yet to be published. Scores derived from the Infant Motor Profile (IMP - Heineman et al., 2008 - primary outcome), the Alberta Infant Motor Scale (AIMS - Darrah et al., 1998 - secondary outcome) and the Teller Acuity Cards (Teller et al. 1986, to test resolution visual acuity-secondary outcome), served as outcome measures. The CareToy System, operated by parents at home and managed remotely by rehabilitation staff, was composed of different modules including sensorized toys, a sensorized mat, interactive walls, an arch, screen and wearable sensors. Parents were guided in promoting different aspects of motor, cognitive, relational and visual development during playtime, for 30 to 45 minutes daily. The rehabilitation staff monitored and adjusted the activities daily, according to specific infant needs and progress. Standard Care consisted of a bi-monthly check-up, during which current care advice on the early management of preterm infants and booklets dedicated to the home-care of preterm infants were distributed. Both the training programs lasted 4 weeks including weekends. After this phase, the infants who started out with Standard Care at T1 were given the opportunity to follow a 4-week CareToy program, and vice versa. Significant positive short-term effects on motor and visual functions (evaluated using the Infant Motor Profile Scale and Teller Acuity Cards, respectively) were reported in the treatment compared to the comparison group. No differences were found for any of the outcome measures in either of the two groups at T2. The CareToy-training wasn't

specifically intended for infants with a diagnosis of VI but rather for infants at risk of VI. The positive improvement in visual acuity wasn't the primary goal of the study. However, it was implemented giving major attention to constant parental involvement with attention to the micro environment concerning the type of objects proposed to the infants during their first months of life. This EI program showed positive short-term effects (4 weeks) on the resolution of visual acuity in infants born preterm, but the lack of a long-term follow-up and the cost of technology limited the generalizability of this program.

Platje and colleagues (Platje et al. 2018) conducted a comparison study on a home-based video-feedback intervention (VIPP-V), previously described in Overbeek and colleagues (Overbeek et al. 2015), specifically designed for families with visually impaired young children. A group of 40 child-parent dyads received VIPP-V integrated with a care-as-usual intervention (CAU) and were compared to 37 dyads who received only CAU. The children were aged between 1 and 5 years and presented visual or visual combined with intellectual disability. No data on the participants' visual profile were reported. Only 3 subjects in the intervention group (8%) and in the comparison group (8%) were defined as "blind". The pretest assessment (T0) took place after randomization and the posttest was performed 7 weeks and 6 months after the intervention. No outcome measures related to visual functions were taken into consideration. Assessments of parental sensitivity and quality of parent–child interaction (primary outcome measures), parenting stress, and parenting self-efficacy (secondary outcome measures) were made in the family home and consisted of computerized questionnaires and a parent–child interactive play task. Families in the CAU group (comparison group) were assessed at the same time points. This therapist-mediated intervention lasted approximately 5 months and was designed to promote positive parenting. VIPP-V consisted of five regular 1.5-hour home-visits, scheduled every 2 to 3 weeks (along

with two booster sessions scheduled every 4–5 weeks) that focused on the original VIPP themes (exploration versus attachment behavior, speaking for the child, sensitivity chain, sharing emotions) and specific added components for parents of children with VI (predictability, safety, independence, making demands, dealing with change and frustration, sharing joint attention, recognizing and naming emotions, empathy and induction). While parental sensitivity or parent–child interaction did not reveal a significant improvement in the intervention group, parenting self-efficacy scores increased and parenting stress rates decreased significantly from pretest to posttest in the treatment group, compared to the comparison group. Regarding the satisfaction of the principles of EI, this study was not proposed in the early months of life (1 to 5 years), limiting the possibility to truly define it as "as early as possible". Moreover, no goal-directed activities promoting visual functions or functional vision or specific details regarding the organization of an enriched environment were described or measured. The VIPP-V however positively contributed to parents' perceptions regarding their overall competence in terms of the basic skills required for taking care of children with VI.

In a comparison study Dale and colleagues (2019) investigated the effects on infants and young children with VI and their parents of receiving home-based EI aimed at improving child developmental and behavioral outcomes and reducing parenting stress. The Developmental Journal for babies and young children with visual impairment (DJVI - Dale & Salt 2007) was given to the enrolled families to monitor and promote developmental progress in play and cognition, social development, language and communication, gross and fine motor skills, independence and autonomy and functional vision. The study was undertaken at a single hospital research site or in-home visits across the UK. Fifty-four families (27 as clinical group with a mean age of 12.9 months and 27 as comparison group with a mean age of 14

months) with full data sets were included in the longitudinal analysis. The disorders of the peripheral visual system were classified as “simple” if no known brain disorders were reported, and “complex” in the presence of a brain lesion/malformation, giving the idea that some infants with CVI were part of the sample. According to the practitioner diary records, families were retrospectively assigned to the DJVI group or to the “Other support” group. Outcome measures, proposed at baseline (T1), 12 (T2) and 24 months (T3) from baseline, included subscales derived from the Reynell-Zinkin scales (Reynell 1978), the evaluation of a developmental setback (defined as the loss of 30 or more developmental quotient points on the Reynell-Zinkin scales), scores on the Total Problem, Emotionally Reactive, and Withdrawn Syndrome subscales derived from the preschool Child Behaviour Checklist (Achenbach 2011), scores on the Total Stress scale, Difficult Child and Parent-Child Dysfunction Interaction subscales derived from the Parenting Stress Index– short form (Abidin 1995), and the mothers’ ratings on the Family-Professional Partnership Scale (Summers et al 2005). The EI protocol, delivered at home or at a nursery with the materials and format of the DJVI, included a comprehensive developmental curriculum of activities and suggestions specifically addressed to VI disability needs and a regular structured developmental monitoring. The EI was mainly provided by qualified specialist teachers (qualified teachers of the visually impaired children) or staff under their supervision. The overall number of visits (at home or nursery) between T1 and T2 was similar between the two samples. An acceleration in sensorimotor understanding and expressive language was reported, especially in the ‘simple’ subsample receiving the DJVI. Vision level (moderate-severe VS profound VI) predicted outcomes. The DJVI group showed improvements in behavioral withdrawal and parenting stress and perceived practitioner–parent relationship. The Dale and colleagues intervention protocol can be considered one of the more recent examples of home-based visual

intervention protocols that shows positive benefits among the families involved. It was conducted during the early months of life, providing goal-directed activities to specifically address and promote visual skills. Parents were also involved in the rehabilitation programs. However, no data on the visual functions monitoring was reported and, as defined by the authors, this was a "low intensity" EI, since the median frequency was about one home visit per month for both groups. Moreover, potential sources of bias were related to the intervention groups' classification that has been defined retrospectively, according to the practitioner diary records of their usual practice over 12 months from baseline.

In 2020 Fontana and colleagues (2020) conducted an RCT to evaluate the effectiveness of an EI program aimed at enhancing visual functions in very preterm infants at risk of VI, without severe morbidities. Infants were enrolled consecutively between 25^{+0} and 29^{+6} weeks of gestational age and randomly allocated to a group that received Standard Care according to the Neonatal Intensive Care Units – NICU -protocols (36 infants) or to the group that received EI (34 infants). Primary outcome measures on visual function were provided through a neonatal visual examination proposed at term equivalent age (Ricci et al., 2008) that evaluated ocular movements, both spontaneous and in reaction to a target, ability to fix and follow a target and to track a colored stimulus, stripes discrimination and visual attention at distance. The visual examination was proposed at the end of the intervention and no data on visual functions were provided before the intervention protocols because of the early nature of the intervention, which was conducted during the patients' stay in the NICU. Standard care, according to the NICU protocol, consisted of Kangaroo Mother Care, nesting and minimal handling, and non-pharmacological pain management. In addition to routine care, the EI protocol included, parental training focused on parental involvement in interpreting the infants' behavior and promoting dyadic interactions, and enriched multisensory stimulation,

through infant massage and visual interaction. The parental training started one week after birth. After three weeks parents started infant massage twice a day and from 34^{+0} weeks of gestational age they started to promote visual interaction once a day. Both interventions were carried out until the term equivalent age. At this age all the infants completed the visual evaluation, which showed significantly better visual performances in the EI group on all the items, reaching a significant level in the "attention at a distance", "stripes discrimination", "ocular movements with target" and "spontaneous ocular motility" scales. This intervention protocol promoted parents' responsiveness to infants' needs and dyadic interaction, emphasizing the importance of a family-oriented approach. However, given the requirement to be conducted at a NICU, no details regarding an appropriate environmental enrichment were provided, nor were measures at baseline collected. Moreover, these positive short-term results are yet without data from a longer follow-up, which is ongoing.

In 2021, a comparison study on the promotion of visual function and general neurodevelopmental skills was carried out by Fazzi and colleagues (2021). In this pilot study, the treatment group was comprised of 30 infants (age range 4–11 months) with VI due to PVI (albinism, Leber's congenital amaurosis or ocular malformation) or CVI. A group of 30 comparison infants matched by gender, age and diagnosis were also incorporated as comparison group. Primary outcome measures were visual acuity, contrast sensitivity and qualitative ocular motor functions, namely fixation, smooth pursuit and saccades, according to the Neonatal assessment Visual European Grid protocol (Rossi et al. 2017). Secondary outcomes were derived from the total and subscale scores on the Griffiths Mental Developmental Scales (GMDS - Griffiths 1996). The training program was delivered at the hospital, at least 3 times per week, for 45 minutes per session, with the involvement of parents and with the aim of promoting visual skills through specific and detailed visual

function training consisting of the accurate adaptation of the micro and macro-environment and the promotion of social interactions (Figure 2). After 6 months, improvement was observed in all the primary outcomes in the treatment group, while the comparison group improved only in visual acuity and contrast sensitivity. Specifically, compared to the comparison group, the treated group showed greater improvement in visual fixation and smooth pursuit. The CVI subgroup showed greater improvement in visual acuity than the PVI subgroup. On the GMDS, Hand-Eye Coordination and Performance scores improved in the treated group, while the comparison group's scores decreased significantly on almost all the subscales.

Despite a number of limitations, such as the heterogeneous nature of the participants' VI, the lack of quantitative accuracy in the evaluation of oculomotor outcomes, and difficulties in controlling for the activities and environmental adaptations of the infants in the comparison group, this study highlighted the importance of implementing an early, intensive, family oriented visual training which, along with environmental adaptations in an interactive context, can lead to improvement in vision-related performance and overall neurodevelopmental outcomes in infants with VI. Because of these limitations, further research is required to verify whether the reported improvements can be sustained, including over a longer period.

Ongoing Trials

In the last 2 years, ongoing study protocols aimed at promoting visual functions in infants and young children with VI have been proposed, with interesting interventions offered to large samples of children living in developing countries (Duke et al. 2019), in large samples of preterm infants (Kooiker et al. 2020) or specifically to children at risk of CVI (Williams et al. 2021).

Only the RCT proposed by Kooiker and colleagues (2020) can be defined as an "early intervention" approach, according to the purposes of this review. The aim of this RCT proposal is to investigate the effectiveness of an EI protocol in promoting visual functions in children born preterm, from 1 year of corrected age. A group of 100 preterm children born at < 30 weeks of GA with visual acuity higher than 0.05 (Snellen equivalent) will be included at around 1 year of CA and identified as at risk or not at risk of VI. A group of 100 typically developing children born at term will be recruited as a comparison group. Children in the comparison group and those in the preterm group with no risk of VI will follow the routine clinical practice, while children born preterm at risk of VI will follow the clinical protocol. Primary outcomes will consist of scores on eye tracking-based visual detection, viewing reaction times, measures of visual acuity, contrast sensitivity, visual field and ocular motility. Secondary outcomes will be total score, cognitive and motor sub scores on Bayley Scales of Infant and Toddler Development. Total score and subscores in the visual domain of the Participation and Activity Inventory for Children and Youth with Visual Impairment Inventory-PAY-CY-0-2 (Elsman et al. 2017) will also be collected. Both measures on visual functions and functional vision will tested at the baseline and at one- and two-year follow-up periods of the study. The visual intervention program will be conducted by therapists from once per week to once per 4-6 weeks. Parents will be encouraged to practice at home with the same exercises proposed during the rehabilitation section. The general protocol will consist of exercises focused on promoting fixation, pursuit, visual attention, visual experience and knowledge, perception of details and visual-motor skills. This study, despite being intended for infants and young children at low risk of VI, shows a well-organized participant allocation and has the potential to provide a solid basis for further intervention protocols designed for infants and young children at risk of VI.

SUMMARY OF THE RESULTS: DIRECTIONS FOR FUTURE RESEARCH

This review provided an overview of the effectiveness of visual intervention programs in infants and young children with VI, either of both peripheral origin or CVI, aged from 0 to 5 years old.

The 9 reported studies raised questions of methodological issues regarding study design, the profile of enrolled participants, the outcome measures employed, the results and the follow-up programs (Table 1 and Table 2); all of which made it very difficult to generate strong scientific evidence and generalizability.

Concerning study design, 5 RCT (Behl 1993; Fontana et al. 2020; Kooiker et al. 2020; Platje et al. 2018; Sgandurra et al. 2017) and 4 comparison studies (Beelmann & Brambring 1998; Dale et al. 2019, Fazzi et al. 2021; Sonksen et al. 1991) have been described.

The participants were heterogeneous including infants with PVI (Beelmann & Brambring 1998; Dale et al. 2019), infants with both PVI and CVI (Fazzi et al. 2021; Sonksen et al. 1991), and infants born preterm with a low risk of VI (Fontana et al. 2020; Kooiker et al. 2020; Sgandurra et al. 2017). In some cases, no data on the causes or symptoms of VI are reported (Behl 1993; Platje et al. 2018). It is known that, despite the presence of some similarities in the phenotypical VI manifestations of ocular and cerebral origin (such as a reduced visual acuity and contrast sensitivity, ocular motor disorders and defects of visual field), the pathways underlying the visual defect may play a relevant role in determining the effectiveness of an early intervention (Bennet et al. 2020; Galli et al. 2022a; Galli et al 2022b; Martin et al. 2016). For example, in the case of PVI, the rest of the downstream processing structures within the brain appear to remain largely intact despite the early loss of visual sensory input, leading to some degree of recovery through compensatory strategies (Martin et al. 2016). On the contrary, the variability in the location and extent of brain injury across

individuals with CVI makes the prediction of visual functional outcomes and recovery particularly challenging (Bennet et al. 2020; Martin et al. 2016). In contrast to their ocular visually impaired peers, children with CVI show clear difficulties in developing adaptive and compensatory strategies (Farrenkopf, et al., 1997) when using assistive technology or existing visual function abilities. As a consequence, the education and rehabilitation strategies developed for people with PVI are not always effective (and even possibly detrimental) for children with CVI (Groenveld et al., 1990; Farrenkopf et al., 1997).

Moreover, beyond the peripheral or central origin of the VI, the specific etiology of disease influences the natural course of the visual disorders as well: for instance, there is a positive evolution in infants and children with CVI associated with PCI or in infants and children with ocular albinism (Galli J et al. 2022a; Galli J et al. 2022b), in contrast with a worsening of clinical conditions in infants and children with Leber Congenital Amaurosis (Huang CH 2021). Thus, the spontaneous developing path of the disease might influence the patient outcome and, if not considered, might lead to mistaken interpretations about the efficacy of the visual intervention.

The outcome measures directly assessed visual aspects in 6 of the reported studies. These included visual functions (Sgandurra et al. 2017, Fontana et al. 2020), functional vision (Beelmann & Brambring 1998) or both visual functions and functional vision (Fazzi et al. 2021; Kooiker et al. 2020; Sonksen et al. 1991). In 3 studies no visual measures (Behl, 1993; Dale et al. 2019; Platje et al. 2018) or no data at baseline were reported (Fontana et al. 2020). The complete assessment of an individual's vision-related abilities may require the consideration and characterization of both visual functions and functional vision that can provide a holistic understanding regarding an individual's visual abilities, as necessary to generate an

appropriate management plan that best suits the needs and developmental goals of an individual (Bennet et al. 2019).

The intervention protocols, conducted by trained therapists (Fazzi et al. 2021; Kooiker et al. 2020) or by parents under therapist supervision (Behl 1993; Dale et al. 2019; Beelmann & Brambring 1998; Fontana et al. 2020; Platje et al. 2018; Sgandurra et al. 2017; Sonksen et al. 1991), took place at home in the majority of cases (Beelmann & Brambring 1998; Behl 1993; Dale et al. 2019; Platje et al. 2018; Sgandurra et al. 2017; Sonksen et al. 1991), incorporating daily and specific activities to be conducted by the parents. Intervention protocols involved direct manipulation or improvement of the child's visual inputs in most of the studies, while two studies (Behl 1993; Platje et al. 2018) used non-vision based interventions that promoted behavioral communication strategies in family contexts. There is substantial agreement over the importance of incorporating the key drivers of neuroplasticity (Novak & Morgan 2019) in the intervention programs, such as the delivery of early individualized training-based interventions harnessing experience-dependent plasticity, supplemented by environmental experiences and in a social context that promotes parent–child interaction measures. These principles have been applied in most of the reported studies.

Regarding the effectiveness of these protocols, encouraging results were described for visual functions or functional vision in most of the studies (Fazzi et al. 2021; Fontana et al. 2020; Sgandurra et al. 2017; Sonksen et al. 1991). In some cases, data were not supported by a baseline assessment (Fontana et al. 2020), the results didn't seem to be robust (Beelmann & Brambring 1998; Behl 1993), or no data are available up to now (Kooiker et al. 2020). The extreme etiological variety of VI described in the reported studies and discussed above, has represented a strong limit for punctual evaluation of the effectiveness of the interventions.

It is also important to note that, in our review, only a few types of treatments were taken into consideration; in particular, those which propose a visual training. Surgical and pharmacological types of interventions or interventions based on visual stimulation were excluded.

This brief summary of the results clearly underlines the broadly heterogeneous nature of the panorama of visual EI, in which there is no clear agreement over not only the length and type of intervention (parent versus therapist mediated), but also the framework that defines the intervention, namely the selection of the clinical population, the recording of specific outcome measures, and the definition of the follow-up programs in order to detect residual visual dysfunctions and continue to promote the general development of children with VI. Given the nature of neuroplasticity, EI programs designed for infants with VI should be implemented by modifying and enriching the natural infant environment, promoting early social interactions, and providing opportunities for multisensorial and motivating experience (Figure 2). The visual intervention should be implemented in a context of active play programs that engage the whole family with the aim to promote not only visual function, but all neurodevelopmental adaptive functions.

CONCLUSIONS

This review supports the need for well-designed, high-quality studies on the effectiveness of early intervention in infants with VI. Encouraging data have been reported on the positive transition towards practice of the principles of EI, in terms of active infant participation in rehabilitative activities, parent involvement in infant care and the provision of rehabilitative activities at home. However, data remain sparse and vague as regards the impact of these protocols on visual functions and functional vision. The lack of consensus in the diagnostic criteria that define VI in pediatric age, with particular regard to CVI, fuels disagreement over

the content of visual intervention programs and, as a consequence, the definition of precise outcome measures. While difficult to implement, further RCTs will provide a high level of scientific evidence regarding the effectiveness of early, intensive, home-based, parent-mediated visual intervention programs for infants with VI or at risk of VI.

LIST OF ABBREVIATIONS

AIMS - Alberta Infant Motor Scale
BDI - Battelle Developmental Inventory
BEB-KV - Bielefeld Developmental Test for Blind Infants and Preschoolers
CAU - care-as usual intervention
CBCL - Child Behaviour Checklist (1y 6mo–5y)
CIH - the curriculum for infants with handicaps developed by the State of Luoisiana
CVI - central visual impairment
EE - enriched environment
EI - early intervention
FACS - Family adaptation and cohesion scales
FRS - Family resource scale
FILEC - Family inventory of life events and changes
FSS - Family support scale
GMDS - Griffiths Mental Developmental scales
IMP - Infant Motor Profile
MA - mean age
NICU - neonatal intensive care unit
PAY-CY 0-2 inventory - Participation and Activity Inventory for Children and Youth with visual impairment
PICO - population, intervention, comparator, outcome
PSI - Parenting stress index
PVD - programme for visual development
PVG - programme for general development
PVI - peripheral visual impairment
RCT - randomized-control trial
ROT - Reach out and teach
RSVC - Response to Sound and Verbal Comprehension
RTC - Reach out and Teach Curriculum
RZS - Reynell-Zinken scales
SMU - Sensorimotor Understanding
VI - visual impairment
VIPP - V Video-feedback intervention to promote positive parenting-visual or visual-and-intellectual disability

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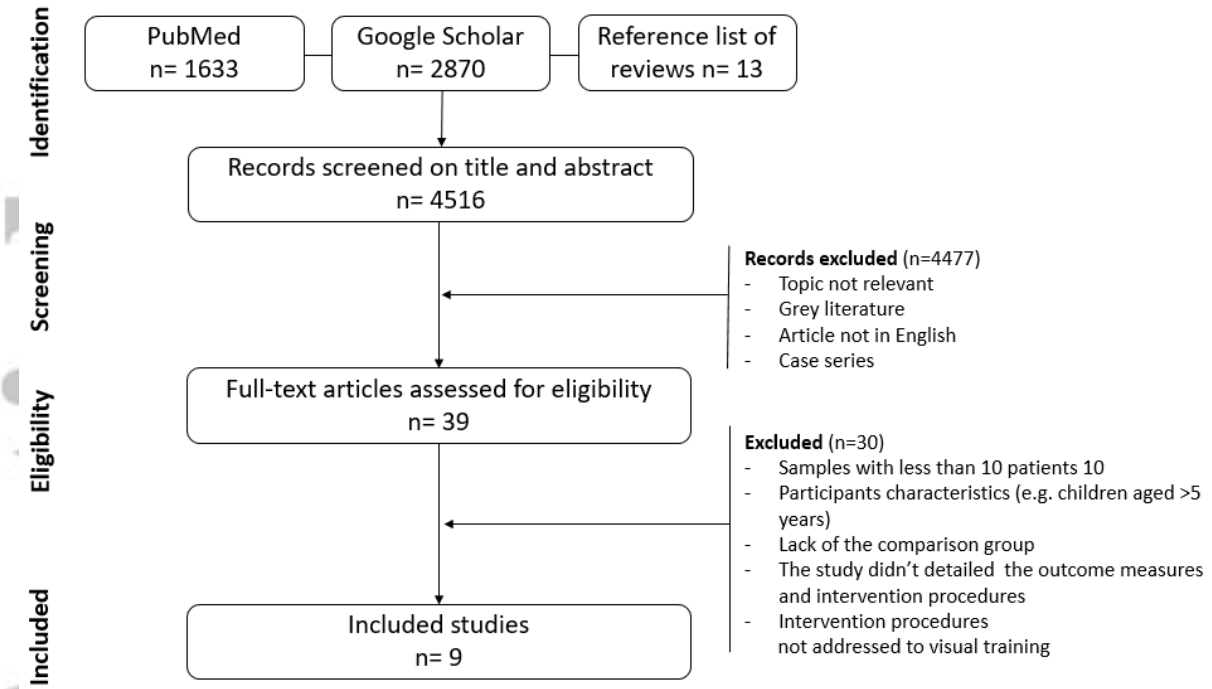

Figure 1. Flow chart showing numbers of studies included and excluded

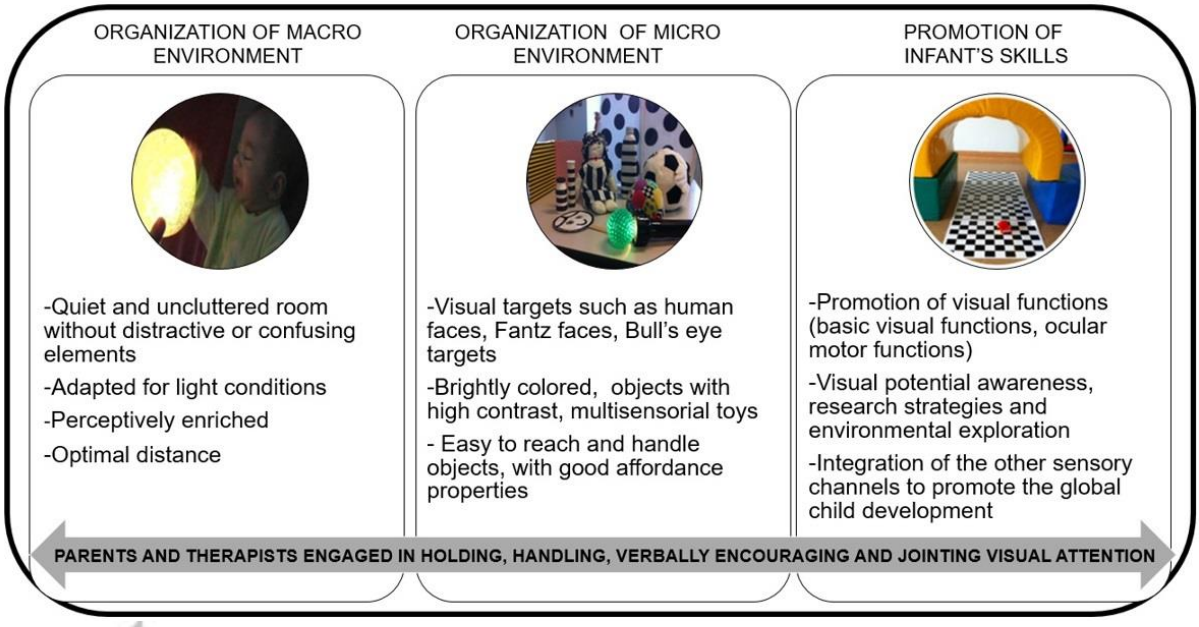

Figure 2: Proposal of the early visual intervention protocol according to Fazzi et al (2021)

TABLE 1: Summary table of the reported studies

	Study design	**sample size[a] (% dropout at last evaluation); MA (age range) in months**	**type of VI (PVI, CVI)**	**outcome measures employed[b] (visual functions/ functional vision/ others)**	**follow-up programs**	**Results** (only significant effects reported)	**Caveats**
Sonksen et al. (1991)	Comparison study	Both prospective randomization and retrospective allocation 58; 35 TG - 23 CG (41% dropout); No MA reported (0-13)	48 PVI 11 CVI	**Visual functions and functional vision** Non-parametric scales on spatial resolution related to acuity, visual following and tracking behaviour, convergence control, visual attention for animate and inanimate stimuli	4 (baseline, after 4-8-12 months)	Higher improvement in TG on near acuity, distant acuity, following horizontal and following vertical scales	High data attrition. Mixture of both retrospective and prospective study design. Protocol evaluation at every 4 months, with no possibility of monitoring the degree of parental support.
Behl et al. (1993)	RCT	Randomized allocation 35; 18 TG – 17 CG (31.5% dropout) MA= 13.8 (2-30)	No data on type of VI, no other major disabilities reported	**Others[c]** BDI Parents and family's functioning: PSI, FSS,FRS,FILEC,FACS	4 (baseline, after 1-2-3 years)	Negligible effects of the high-intensity intervention on child and family functioning	No details on visual-specific activities. No outcome measures regarding visual aspects.
Beelmann & Brambring 1998	Comparison study	Convenience sampling 50; 10 TG – 40 CG No dropout reported MA[d]= 12 (9.5-19) No MA reported in CG (12-36 CG)	PVI	**Functional vision** BEB-KV	6 (12,15,18,24,30,36 months of infants' ages)	12 to 36 months increased scores at BEB-KV in the full-term children. No effects found in the preterm children	Non-homogeneous selection of participants at baseline in terms of severity and causes of VI. No measures of visual functions.
Sgandurra et al. 2017	RCT	Randomized allocation 41; 19 TG – 22 CG (0% dropout)	Preterm infants at risk of PVI/CVI	**Visual functions** Visual acuity by Teller Acuity Cards **Others**	3 (Baseline, after 4 weeks and after 4 weeks from re-allocation)	Higher scores in TG in IMP (total score, Performance and Variation subdomains) and visual acuity	Lack of a long-term follow-up. The cost of technology could limit the generalizability of this program.

		MA= 3.9 (3.0-5.9)		IMP; AIMS			
Platje et al. 2018	RCT	Randomized allocation 77; 40 TG – 37 CG (11% dropout) MA TG= 36.36 (12.2[e]) MA CG= 36.22 (12.02[e])	No data on type of VI	**Others** Parental sensitivity, quality of parent-child interaction, parenting self-efficacy, parenting stress	3 (Baseline, 7 weeks and 6 months after the intervention)	At posttest, lower parenting stress in TG and higher parenting self-efficacy in TG	Not proposed in early months of life. No goal-directed activities promoting visual functions or functional vision.
Dale et al. (2019)	Comparison study	Retrospective allocation 54; 27 TG, 27 CG (14.2% dropout) MA TG= 12.9 (2.6[d]) MA CG= 14.0 (1.96[e])	PVI, CVI probably present in the "complex" VI but not specifically reported	**Others** RZS; CBCL, PSI	3 (baseline, 12 and 24 months after baseline	Higher improvements in TG compared to CG in behavioural withdrawal, in parenting stress and in perceived practitioner–parent relationship	No monitoring of visual functions; "Low intensity" EI. Intervention groups' classification defined retrospectively, according to the practitioner's records.
Fontana et al. (2020)	RCT	Randomized allocation 70; 34 TG; 36 CG (18% dropout) MA TG=26.4[h] (0.9[e,f]) MA CG=27.8[h] (1.3[e,f])	Preterm infants at risk of PVI/CVI	**Visual functions** Visual assessment protocol developed by Ricci et al (2008)	1 At term equivalent age	Higher scores in TG in five out of nine items of the visual protocol	No details on environmental enrichment (intervention conducted at a NICU). No measures at baseline. No long follow-up; currently ongoing.
Fazzi et al. (2021)	Comparison study	Convenience sampling 60; 30 TG; 30 CG (0% dropout) MA TG=5.2 (4-11) MA CG=6 (4-9)	30 PVI (15 TG, 15 CG) 30 CVI (15 TG; 15 CG)	**Visual functions** Basic-visual (visual acuity, contrast sensitivity) and ocular motor (fixations, smooth pursuit and saccades) functions **Others** GMDS	2 (baseline, 6 months after baseline)	Higher improvement in TG in visual fixation and smooth pursuit. At GMDS Hand-eye coordination and Performance subscales improved in TG Visual acuity better improved in infants with CVI, compared to infants with PVI	Heterogeneous nature of participants' VI. Lack of quantitative accuracy in the evaluation of oculomotor outcomes. Difficulties in controlling for activities and environmental adaptations of the infants in the comparison group

Kooiker et al. (2020)	RCT	Randomized allocation TG= about 50 expected CG= about 150 expected	Preterm infants at risk of PVI/CVI	**Visual functions and functional vision** Visual screening by eye-tracking Visual behavior inventory; PAY-CY 0-2 inventory **Others** Bayley Scales of Infant and Toddler Development III	3 (Baseline, 1 year and 2 years after baseline)	Not available yet	NA

[a]data analyzed
[b] measures that underwent to a statistical comparison
[c]no measures underwent to a longitudinal comparison
[d]only for TG
[e]standard deviation
[f]gestational age

LEGEND: TG= treatment group, CG= comparison group; MA= mean age; PVI= peripheral visual impairment; CVI= central visual impairment; RCT= randomized-control trial; BDI=Battelle Developmental Inventory; PSI= Parenting stress index; FSS= Family support scale; FRS=Family resource scale; FILEC= Family inventory of life events and changes, FACS= Family adaptation and cohesion scales; BEB-KV=Bielefeld Developmental Test for Blind Infants and Preschoolers including 6 scales assessing general development (neuromotor skills, cognition, language, socioemotional development) and blindness-specific development (orientation and mobility, fine motor and daily living skills); IMP= Infant Motor Profile; AIMS= Alberta Infant Motor Scale; sd= standard deviation; VIPP-V= Video-feedback intervention to promote positive parenting-visual or visual-and-intellectual disability; RZS=Reynell-Zinken scales; CBCL= Child Behaviour Checklist (1y 6mo–5y); GMDS=Griffiths Mental Developmental scales; PAY-CY 0-2 inventory=Participation and Activity Inventory for Children and Youth with visual impairment

TABLE 2: Type of intervention program

	CONTENTS	LOCATION	PROVIDERS	FREQUENCY (DURATION)
Sonksen et al. (1991)	**TG** PGD + PVD **CG** PGD	**TG -CG** At home, activities to incorporate into daily play and routines	**TG - CG** Parents supported by the researcher after each assessment	**TG-CG[a]** home visits by therapists were not reported and the established evaluation of the protocol was set at every 4 months, (12 months)
Behl et al. (1993)	**TG** Tailored parent-infant sessions incorporating daily routines, CIH, ROT **CG** General stimulation activities provided during meetings	**TG** At home **CG** Group meetings (not specified where), at home	**TG - CG** Parents supported by the researchers	**TG[a]** 1 time/week for 60 minutes, (19.6[e] months) **CG** 12 times/ year, (20[e] months)
Beelmann & Brambring 1998	**TG** Exercises on fine and gross-motor behavior, orientation cognition, residual vision, other areas of promotion PLUS parent counseling **CG** Usual care by the regional blind-specific centres	**TG-CG** At home	**TG-CG** Parents supported by the researchers/ therapists	**TG[a]** 1 time/2 weeks for about 3 hours, (24[e] months) **CG** No data are available
Sgandurra et al. 2017	**TG** Caretoy System **CG** Follow-up check with distribution of booklets dedicated to home-care of preterm infants	**TG** At home **CG** At the Hospital	**TG** Parents remotely monitored by the researchers/ therapists **TG - CG** Parents supported by the researchers	**TG** Daily for about 30-45 minutes, (4 weeks) **CG** Bimonthly follow-up
Platje et al. 2018	**TG** VIPP-V PLUS care-as-usual intervention **CG**	**TG** At home **CG**	**TG-CG** Parents supported by the researchers	**TG[a]** 7 sessions/2-5 weeks for about 90 minutes per session, (5 months)

	Care as usual intervention	At home (not clearly specified)		**CG** Not specified
Dale et al. (2019)	**TG** DJVI or DJVI PLUS other supports **CG** Other supports	**TG-CG** At home and at nursery	**TG-CG** Parents supported by the researchers	**TG**[a] 12 sessions/ year[e],(12 months) **CG**[a] 13.0 sessions/ year[e],(12 months)
Fontana et al. (2020)	**TG** Routine care according to NICU protocols PLUS parental training on promoting dyadic interactions PLUS enriched multisensory stimulation **CG** Routine care according to NICU protocols	**TG-CG** At the hospital (NICU)	**TG-CG** Parents supported by the researchers	**TG** Infant massage twice/day; visual interaction promotion once/day, (about 8 weeks) **CG** no data available
Fazzi et al. (2021)	**TG** Promotion of visual skills and neurodevelopment through adaptation of the environment, promotion of social interactions and a structured visual functions training **CG** Routine treatment from local health care providers PLUS clinical follow up	**TG** At the hospital **CG** At the hospital	**TG** Therapists who encourage parents to practice at home **CG** Parents supported by a researchers	**TG**[a] At least 3 times/ week, for 45 minutes per session **CG** Clinical follow up one time/month
Kooiker et al. (2020)	**TG** General visual protocol promoting fixation, pursuit, visual attention, visual experience and knowledge, perception of details and visual-motor skills PLUS an individualized protocol tailored to the specific VI of the child **CG** General developmental support and monitoring	**TG** At the hospital **CG** Not specified	**TG** Therapists who encourage parents to practice at home **CG** Parents supported by a researchers	**TG** From once/week to once/4-6 weeks by the therapists (about 12 months) **CG** Not specified

[a] parents are encouraged to practice daily

[b] average length (frequency or duration)

PGD= programme for general development consisting in individualized ideas to promote many aspects of general development; PVD= programme for visual development consisting in individualized and flexible activities and visual lures, within a structured framework to promote visual development; CIH= The curriculum for infants with handicaps developed by the State of Louisiana; ROT= Reach out and teach; DJVI: Developmental Journal for babies and young children with visual impairment; NICU=Neonatal intensive care unit

There is the need for well-designed, high-quality studies on the effectiveness of early visual intervention protocols in infants with visual impairment or at risk of visual impairment. There protocols should include an active infant participation in rehabilitative activities, parent involvement in infant care and the provision of rehabilitative activities at home.

			
STUDY DESIGN		-randomized clinical trials	-type of randomization
SUBJECTS		-infants with visual impairment of peripheral origin or caused by a cerebral visual impairment	-infants at risk of visual impairment -type of VI (CVI and/or PVI) -causes of visual impairment -directly addressed to infant or indirectly addressed to the parents who act with the infant
OUTCOME MEASURES		-objective and measurable (statistical analysis is strongly recommended) -considering both visual function and functional vision -evaluated before and after the treatment	-length of monitoring -consensus of measures to evaluate functional vision
INTERVENTION PROTOCOLS	WHEN	-as early as possible	-frequency/ intensity
	WHERE	-environmental modification and adaptation in a social context	-place where the sessions are conducted (whether at home or at clinical services)
	WHO	-importance of parental involvement	-parent mediated approach versus therapist mediated approach
	WHAT	-individualized activities harnessing experience-dependent plasticity incorporating daily activities	-visual stimulation versus visual training