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Effect of early multisensory massage intervention on visual functions in infants with Down syndrome

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ABSTRACT

Background: Down syndrome is a frequent cause of intellectual disability, with severe impact on the quality of life of affected individuals and their families, and high social costs. Intervention programs should start soon after birth but no consensus exists on specific types and timing of early interventions in this population.
Aim: This pilot study explores the effects of an early multi-sensory intervention, based on body massage, on the development of visual function in infants with Down syndrome.
Method: Infants were randomly allocated to either a massage or a control group. Intervention consisted of only standard care (Control Group) or standard care plus infant massage (Massaged Group). Visual acuity was assessed by Teller Acuity Cards and stereopsis by the Frisby Stereopsis Screening Test at 5, 6, 9 and 12 months.
Results: Massaged Group Infants showed a significantly higher visual acuity at 6 months of age and an accelerated development up to at least 12 months; compared to Controls, stereopsis had an earlier onset in the Massaged Group followed by a faster maturation.
Conclusion: Environmental enrichment, in the tested form of infant massage, seems to affect maturation of visual functions in human infants, also in the presence of a genetic disability, when applied during a period of high brain plasticity.

1. Introduction

Down syndrome (DS) is the most common genetic cause of intellectual disability, with an incidence of more than 1 in 1000 new births [1]. The impact of cognitive and sensorial deficits on quality of life of affected individuals and their families is remarkable, with high cost for the National Health System. It is widely suggested that intervention programs should start soon after birth, in order to support brain developmental processes in a period of relatively high plasticity and influence long-term outcomes [2]. Unfortunately, due to a lack of both clinical and experimental data, no consensus exists on specific types and timing of early interventions in this population.

The environmental enrichment (EE) paradigm seems to be promising as an early and non-invasive strategy for positive brain plasticity in newborns with neurodevelopmental disorders [3]. EE is defined as a combination of complex inanimate stimulation and social stimulation [4] and as a condition of increased sensory–motor stimulation [3]. The beneficial effects of early EE programs on several aspects of brain development and brain plasticity have been well described recently in animal models, in particular in mouse pups, both in wild types and in lines modeling human congenital disabilities [5]. The modulation of expression of crucial molecular mediators, such as IGF-1 and BDNF, has been identified as a key mechanism mediating EE effects and also confirmed in human conditions. Moreover, it has been recently reported that in a mouse model of DS, Ts65Dn line, increased sensory–motor stimulation in adulthood through EE reduces brain inhibition levels and promotes recovery of some abilities, including visual functions [6].

EE in mice by sensory–motor stimulation is similar to the technique of infant massage (IM) in humans. IM not only is a standardized model of mainly tactile stimulation, but also is proprioceptive and mediated by other sensors, provided by caregivers' hands, consisting of gentle, slow stroking of each body part, which is currently widely diffuse in neonatal care. Evidence of the significant effects of IM on weight gain rate, on stress hormone levels such as cortisol, on growth hormone [7], and on IGF-1 [8] is available in newborns and infants. In preterm infants, it has been shown that body massage influences visual development and affects maturation of cerebral electrical activity [9,10]. In these infants, tactile stimulation probably plays a positive role in neurodevelopment similar to that observed in utero in term infants.

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Our hypothesis was that EE by IM produces a positive effect on the neurodevelopment of infants with DS, supporting and accelerating visual function maturation, which during infancy has an important role for the development of cognitive and social-communication competencies.

The rationale for testing a paradigm of early EE in very young infants with DS is that early environmental experience of these infants is at high risk of being suboptimal for several reasons. In particular, prolonged hospitalization, as well as effects of diagnosis on parent–infant bonding and parents' mood and anxiety, could compromise early parent–infant relationship and thus hinder the quality of environmental stimulation offered [11].

Given the growing consensus on the effectiveness of IM as a paradigm of EE in humans, it is crucial to study its application and effectiveness as a form of early intervention on different clinical populations. To address this issue, we have explored the effects of IM on brain development and in particular on visual system development in a group of DS infants.

2. Methods

2.1. Participants

Twenty infants with DS, 14 males and 6 females, born between 2010 and 2012, participated in this study. Initially, 30 infants had been enrolled but four were excluded due to subsequent severe clinical problems and six due to poor compliance.

All the infants were recruited between 1 and 3 months of age and have been longitudinally followed up in Pisa at the Department of Developmental Neuroscience, Stella Maris Foundation.

All subjects were randomized into two intervention groups. A group of Massaged Infants, consisting of 10 subjects (9 trisomy 21 and 1 translocation), received IM performed by a parent in addition to standard care; a Control Group, consisting of 10 infants (9 trisomy 21 and 1 mosaicism), received only the standard care without IM. The standard care consisted of a bi-monthly parent counseling made by the professionals of our team. The study was approved by the Ethics Committee of the Stella Maris Scientific Institute; informed consent for participation was obtained from parents of all subjects. The study was conducted in accordance with the Declaration of Helsinki.

2.2. Type of intervention

IM is a complex practice, centered on the idea of fostering and facilitating mother–infant bonding and mother–infant relationship through different components: skin-to-skin contact, kinesthetic stimulation, and mother and infant pre-verbal communication (eye-contact, social smiling, mimicking expressions, recognition and interpretation of infant's communicative cues and body language). IM was taught by a Certified Infant Massage Instructor (CIMI) according to the International Association of Infant Massage (IAIM®) in 5 weekly classes starting between two and four months of life. Parents were invited to perform massage sessions one time per day, while the infant was in quiet or in active alertness, at least up to the sixth month of life. Each treatment session consisted approximately of 15 min of tactile stimulation, followed by 5 min of kinesthetic stimulation. The head, neck, shoulders, buttocks, and both legs and arms were stimulated. For the kinesthetic phase, the infant was placed in a supine position and parents applied passive flexion/extension movements of the limbs.

2.3. Battery for evaluation of visual development

The development of visual functions during the first year of life is very rapid and represents a good marker of the influence of environment on the global development of the infant [12].

To study the effect of IM on the two groups, we evaluated visual acuity and stereopsis at 5, 6, 9 and 12 months. These tests were administered by two clinicians (G.P. and F.T.), blinded for group assignment and expert in children visual assessment.

Visual acuity, assessed by means of *Teller Acuity Cards* (TACs) [13], was selected as the main outcome measure since a previous study by Guzzetta et al. [10] showed that IM determined many positive changes on the development of visual acuity in infants at risk of neurodevelopmental disorders.

This test is based on a preferential looking paradigm, i.e., spontaneous behavioral reaction of newborns and infants consisting of gazing or turning of head toward the most salient of two or more alternative visual stimuli [14]. TACs were used in a number of studies including populations with several neurodevelopmental disorders (i.e., cerebral palsy, mental retardation) and performances were considered unaffected by general cognitive level of subjects [15]. The stimulus consists of a series of stripes (grating) displayed on cards, and acuity value is defined by the smallest stripe width that consistently elicits a preferential looking response. The examiner presents gratings in an increasing spatial frequency order (from 0.32 to 38 cycles/cm) and judges infant reaction to the location of test stimulus on the basis of eye and head movements. Viewing distance is set at 40 or 57 cm, according to patient age. Acuity values are expressed as cycles per degree and can be compared to normative data [15–17].

Stereopsis is the highest form of binocular coordination that can be assessed [18]. Despite the wide variety of visual stimuli (contour and random dot, static and dynamic) and response measures (forced-choice preferential looking, visual evoked potential, and eye movements) used in various studies, there is a general agreement that the onset of stereopsis in typically developing infants occurs at 3 to 4 months of age [19]. Stereopsis is an important index of cortical maturation because its development is mediated by the cortical area, even if till now it is not clear which area is specifically involved in stereopsis processing [20].

In this study it was evaluated by means of the *Frisby Stereopsis Screening Test* [21]. Briefly, the participant's task is to detect a circle containing a pattern of geometric objects (target) visible within a mosaic of similar geometric shapes. The target and background are printed on opposite sides of a Perspex plate and so differ in physical depth. Angular disparity depends on the thickness of the plate and the distance from the observer. The Frisby Test comprises three plates, each of which can be presented at one of several different possible distances to obtain a range of disparities. A positive result is recorded if the subject's scanning eye movements stop consistently at the correct target upon repeated testing. Stereopsis values are expressed as s/arc. Participants who could not identify a target at 600 s/arc were classified as stereonegative. For our convenience, we identified “0” as no stereopsis; “1” as a stereopsis of 600 s/arc, “2” as a stereopsis of 300 s/arc and “3” as a stereopsis of 150 s/arc.

2.4. Statistical analysis

Comparison of the Massaged Group (Group M) to the Control Group (Group C) at 5, 6, 9 and 12 month examinations for clinical continuous factors (Teller Acuity Card score) was performed by using independent T test, while the corresponding non-parametric Mann–Whitney U test analysis was employed for clinical categorical factors (Frisby Stereopsis Screening Test score).

For clinical continuous factors (Teller Acuity Card score) repeated measure analysis of variance (rm-ANOVA) models and post-hoc tests (*Bonferroni*) were performed. Moreover, the multi-step statistical analysis based on linear mixed models was applied for assessing response to IM by Teller Acuity Card score.

With rm-ANOVA it is not possible to evaluate the time-course of every variable for each patient, therefore the subsequent step of statistical analysis was a multiple regression analysis for repeated measures