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## Time, number and attention in very low birth weight children



Francesca Tinelli <sup>a</sup>, Giovanni Anobile <sup>b</sup>, Monica Gori <sup>c</sup>, David Aagten-Murphy <sup>d</sup>, Mariaelisa Bartoli <sup>a</sup>, David C. Burr <sup>b,e,\*</sup>, Giovanni Cioni <sup>a,f</sup>, Maria Concetta Morrone <sup>a,g</sup>

- <sup>a</sup> Department of Developmental Neuroscience, Stella Maris Scientific Institute, Pisa, Italy
- <sup>b</sup> Department of Neuroscience, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy
- <sup>c</sup> Robotics, Brain & Cognitive Sciences Department, Istituto Italiano di Tecnologia, Genoa, Italy
- <sup>d</sup> Department of Psychology, Ludwings-Maximilians University, Munich, Germany
- <sup>e</sup> CNR Institute of Neuroscience, Pisa, Italy
- <sup>f</sup> Department of Clinical and Experimental Medicine, University of Pisa, Italy
- g Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Italy

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#### ABSTRACT

Premature birth has been associated with damage in many regions of the cerebral cortex, although there is a particularly strong susceptibility for damage within the parieto-occipital lobes (Volpe, 2009). As these areas have been shown to be critical for both visual attention and magnitudes perception (time, space, and number), it is important to investigate the impact of prematurity on both the magnitude and attentional systems, particularly for children without overt white matter injuries, where the lack of obvious injury may cause their difficulties to remain unnoticed. In this study, we investigated the ability to judge time intervals (visual, audio and audio-visual temporal bisection), discriminate between numerical quantities (numerosity comparison), map numbers onto space (numberline task) and to maintain visuo-spatial attention (multiple-object-tracking) in school-age preterm children (N29). The results show that various parietal functions may be more or less robust to prematurity-related difficulties, with strong impairments found on time estimation and attentional task, while numerical discrimination or mapping tasks remained relatively unimpaired. Thus while our study generally supports the hypothesis of a dorsal stream vulnerability in children born preterm relative to other cortical locations, it further suggests that particular cognitive processes, as highlighted by performance on different tasks, are far more susceptible than others.

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#### 1. Introduction

The ability of our visual system to estimate the number, time or spatial extent of visual objects in the world has been traditionally thought of as independent and distinct mechanisms. However, recent work has begun to suggest that a common cortical metric is responsible for the processing those features (a theory of magnitude "ATOM", see Walsh (2003), and proposed that the parietal cortex is the crucial brain area for this goal. As the parietal cortex is particularly vulnerable to early injuries, especially in preterm subjects (Volpe, 2009), it is of great importance whether injury, even sufficiently minor to typically pass undetected, could result in subtle difficulties for individuals with any kind of magnitude judgement.

Even in the absence of evident brain lesions, preterm children show impairments in a variety of different visuo-spatial abilities. This includes performance on tasks designed to investigate selective, sustained, shifting or divided-attention (Anderson et al., 2011; de Kieviet et al., 2013; Potharst et al., 2013) as well as tasks investigating both local and global motion (Guzzetta et al., 2009; MacKay et al., 2005; Taylor et al., 2009). Crucially, the current literature suggests that all these functions occur primarily in the parietal cortex (Bueti and Walsh, 2009). Recently, clinical research investigating parietal functioning and the impact of premature birth has focused on a subgroup of preterm children. characterized by a very low birth-weight (less than 1500 g; VLBW), representing 1-5% of all live-births. These children suffer an exceptionally high risk of death or extensive brain lesions. If they survive, even without major neural deficits, they very often encounter more "subtle" symptoms such as academic underachievement (Rodrigues et al., 2006; Taylor et al., 2009), behavioral problems (Bhutta, et al., 2002; Hack et al., 2004; Saigal et al.,

<sup>\*</sup> Corresponding author at: Department of Neuroscience, Psychology, Pharmacology and Child Health, University of Florence, Florence, Italy.

E-mail address: dave@in.cnr.it (D.C. Burr).

2003) and deficits in higher-order neurocognitive functions such as executive functions (Ni et al., 2011).

Although a large variety of these less direct symptoms have been reported, visuospatial abilities (particularly those related to magnitude) may be common to many of them and represent a root cause. Indeed preterm children often undergo school achievement problems (Rodrigues et al., 2006; Taylor et al., 2009), particularly impacting on the acquisition of mathematical achievements (Taylor et al., 2009). Two different mechanisms have been proposed to underlie number representation (Castronovo and Gobel, 2012), an approximate number system (ANS) and an exact number system (ENS). The first, functional from very early, preverbal age. allows fast and approximate estimations of sets of objects, without requiring serial counting. In contrast the ENS refers to formal school-acquired mathematical education and knowledge of symbolic numbers. ANS precision (often reported as 'number acuity') has been shown to greatly improve throughout development (Piazza et al., 2013) and has furthermore been demonstrated to be a good predictor for future (Halberda and Feigenson, 2008) and current formal mathematics achievement in children (Anobile et al., 2013; Chen and Li, 2014; Halberda et al., 2008; Mazzocco et al., 2011).

The neural substrate supporting both the approximate and the exact number systems has been localized predominately within parietal-frontal regions (Butterworth and Walsh, 2011; Dehaene et al., 2003; Eger et al., 2009) with the intraparietal sulcus (IPS) identified as the as the locus for such processes (Kaufmann et al., 2011). The IPS has also been identified as the brain area where number and space interact (Hubbard et al., 2005). Indeed humans have a strong intuition of the spatial representation of numbers, with this spatial relationship often expressed as a mental numberline with numbers increasing from left to right (Hubbard et al., 2005). However, this mental numberline is not static throughout development (Booth and Siegler, 2006; Siegler and Booth, 2004; Siegler and Opfer, 2003). Kindergarten children have been shown to represent numbers in space in a compressed, seemingly logarithmic, scale (placing the number 10 near the midpoint of a 1-100 scale). As children mature (and experience the first three or four years of formal education) this scale becomes progressively more accurate (linear) and the degree of the accuracy has been found to positively correlate with children's mathematical skills (Halberda and Feigenson, 2008).

Similarly to how numerical estimation has been shown to have strong links to the spatial representation of numbers (numberline), visual attention has also been shown to interact with many aspects of numerosity and numerical cognition (Sathian et al., 1999). Indeed, simply looking at different numbers can cause a shift either to the left or right in covert attention, depending upon the magnitude of the number (Fischer et al., 2003). Furthermore, the capacity to quickly estimate small sets of items (subitizing) employed by the ENS, as well as the ability to map numbers onto space (numberline) have both been shown to require visual attention (Anobile et al., 2012; Railo et al., 2008; Ross and Burr, 2010; Vetter et al., 2008). Anobile et al. (2013) investigated the relationship between formal mathematical skills, the perception of numerosity (discrimination and mapping to numberline) and visual sustained attention in school age children (from eight to 11 years). The results showed that formal math skills correlated with numerosity discrimination precision, number-to-space mapping (numberline task) and with visual attention capacity. Interestingly, attentional performance remained correlated with formal math skills after controlling for age, non-verbal intelligence, gender and reading accuracy.

Walsh (2003) has proposed that numerical and temporal information are processed by partially overlapping magnitude systems. In a recent study, Hayashi et al. (2013) used fMRI in humans

to show that the right intra-parietal cortex (IPC) and inferior frontal gyrus (IFG) are jointly activated by duration and numerosity discrimination tasks, with a congruency effect in the right IFG. Using transcranial magnetic stimulation and two different numerosity—time interaction tasks, they demonstrated that the right IFG is specifically involved at the categorical decision stage, whereas interaction of numerosity with perception of time occurs within the IPC. Taken together, there is abundant evidence for a strong connection between the representations of numbers, time, space and attention in children with typical development.

Given that impairments in mathematical and other dorsal-stream-mediated skills have been widely reported in preterm children, especially in those born with VLBW, we believe that preterms represent an interesting population to investigate the perception of magnitude-related features, as well as attention. Surprisingly, to our knowledge, the literature on this topic is limited to few studies: one that investigates basic numerical processes in very preterm children (Guarini et al., 2014) and another about numerosity discrimination in extremely preterm school-aged children (Hellgren et al., 2013) and a very recent paper (Skagerlund and Traff, 2014) showing a general magnitude processing deficit (space, time and number) in children with developmental dyscalculia.

In this study we measured performance on time estimation, visual numerosity perception, number-to-space mapping (numberline) and sustained visual attention in a group of VLBW children and age-matched controls. In brief, our results confirm the vulnerability of the dorsal stream in children born preterm (VLBW), and further show that the degree of vulnerability is specific for particular tasks processed through this neural pathway, rather than applying uniformly to all tasks.

#### 2. Materials and methods

#### 2.1. Participants

This study was conducted under ethical approval from the Stella Maris Scientific Institute Ethics Committee. Preterm children were enrolled from a population based follow-up study and consisted of a group of children born with VLBW. The enrolment was done if they met the following criteria: (1) gestational age at birth below or equal to 32 weeks and birth-weight less than or equal to 1500 g; (2) absence of any major cerebral damage: normal results at postnatal brain ultrasound or periventricular increased echo density persisting less than 14 days and being less than or equal to grade I of De Vries' classification (de Vries et al., 1992) and/or intraventicular hemorrhage (IVH) grade I according to Papile et al. (1978); (3) absence of motor impairment or other specific disorders at neurological examination; (4) no congenital malformations; (5) absence of major ocular anomalies such as cataracts, optic atrophy and retinopathy of prematurity > II grade, and a binocular visual acuity above 0.4 logMAR (20/50 Snellen acuity); (6) no auditory impairment (a hearing exam was done to all subjects within 1 year of age ); and (7) age ranging from 6 to 11

Forty-five families of VLBW children born between January 2001 and December 2003 were contacted by phone. Thirty families gave their consent to the enrolment of their children in the study (i.e. 67%) but only 29 of them (97%) satisfied the inclusion criteria. One subject was eliminated from the study as their attentional span was insufficient to complete the task.

Controls consisted of term-born children with a birth-weight more than 2500 g recruited from the local schools and matched to the preterm group in both gender and age.

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