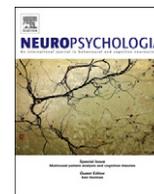




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Impaired visual size-discrimination in children with movement disorders

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ABSTRACT

Multisensory integration of spatial information occurs late in childhood, at around eight years (Gori, Del Viva, Sandini, & Burr, 2008). For younger children, the haptic system dominates size discrimination and vision dominates orientation discrimination: the dominance may reflect *sensory calibration*, and could have direct consequences on children born with specific sensory disabilities. Here we measure thresholds for visual discrimination of orientation and size in children with movement disorders of upper limbs. Visual orientation discrimination was very similar to the age-matched typical children, but visual size discrimination thresholds were far worse, in all eight individuals with early-onset movement disorder. This surprising and counterintuitive result is readily explained by the cross-sensory calibration hypothesis: when the haptic sense is unavailable for manipulation, it cannot be readily used to estimate size, and hence to calibrate the visual experience of size: visual discrimination is subsequently impaired. This complements a previous study showing that non-sighted children have reduced acuity for haptic orientation, but not haptic size, discriminations (Gori, Sandini, Martinoli, & Burr, 2010). Together these studies show that when either vision or haptic manipulation is impaired, the impairment also impacts on complementary sensory systems that are calibrated by that one.

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1. Introduction

It is generally assumed, with good supporting evidence, that individuals with a specific sensory disability – such as blindness – will show enhanced sensitivity in their other senses. For example, blind people have enhanced auditory sensitivity (e.g., Lessard, Pare, Lepore, & Lassonde, 1998; Muchnik, Efrati, Nemeth, Malin, & Hildesheimer, 1991; Roder et al., 1999) and also better tactile and haptic discriminations for many tasks (e.g., Alary et al., 2009; Sunanto & Nakata, 1998). The enhanced sensitivity could arise from cortical reorganization, as suggested by imaging studies. For example, a strong BOLD response to auditory motion in visual-motion area MT+ has been reported for in congenitally blind subjects (Bedny, Konkle, Pelphrey, Saxe, & Pascual-Leone, 2010), and a visual response in auditory cortex A1 in deaf people (Finney, Fine, & Dobkins, 2001). Animal deprivation studies show similar results, both behaviorally and electro-physiologically (Rauschecker, 1995).

Results suggesting compensatory sensitivity in the surviving senses are intuitively appealing, consistent with the notion of a

flexible neural system that makes full use of cortical regions vacated by other senses, as well as the fact that people deprived of one sense will necessarily compensate with, and hence over-practice the others. However, there are also reasons to expect the results to go the other way, in certain specific cases. An important role for cross-sensory interactions is *calibration* of sensory systems. This idea goes back to George Berkeley's maxim that "touch educates vision" (Berkeley, 1709/1963). Many studies point to the importance of cross-sensory calibration. Many classical studies have described cross-modal interactions in a visuo-motor coordination task (for a review see Harris, 1965). Most recently, Wozny and Shams (2011) have shown that just one brief audio-visual presentation of a stimulus can bias the perceived direction of subsequent sounds. Recently, we have suggested that cross-sensory calibration may be particularly important in the developing child (Burr, Binda, & Gori, 2011; Burr & Gori, 2011). Whereas adults integrate signals from different senses – such as haptic and visual cues – in a way that can be shown to be *statistically optimal* (Ernst & Banks, 2002), young children do not (Gori et al., 2008). In children younger than eight years, one sense dominates the other, depending on the task: for size judgments the haptic system dominates vision, but for orientation judgments vision dominates the haptic modality. We suggested that the reason for the lack of sensory fusion in young children may be

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that in the developing brain the senses are being continually calibrated, and cross-sensory information is a particularly important form of calibration; and if one sense is calibrating the other, the redundant sensory information between them cannot be integrated to improve precision.

This leaves the question of why vision should calibrate (and hence dominate) orientation judgements, while haptic signals calibrate and dominate size judgments. There is now a clear consensus that fusion of cross-sensory information in adults usually depends on the relative *reliability* of the various signals: when in conflict – either for natural or experimentally induced reasons – the resulting perception is given by the weighted average of the signals, with weights proportional to relative reliability. It is simple to demonstrate that this combination rule optimizes performance (e.g., Landy, Banks, & Knill, 2011) and it has been verified experimentally in many laboratories for many sensory modalities (e.g., Alais & Burr, 2004; Ernst & Banks, 2002; Ghahramani, Wolpert, & Jordan, 1997; Hillis, Watt, Landy, & Banks, 2004; Knill & Saunders, 2003; Landy & Kojima, 2001; Tassinari, Hudson, & Landy, 2006). And the idea makes good intuitive sense: if the goal is increase reliability the more reliable signals should receive more weight. It is less clear which sensory signals should govern cross-sensory calibration. Ghahramani et al. (1997) suggested – with evidence – that reliability should also determine calibration, but theoretical reasoning behind this argument is less clear. Reliability is a measure of *precision*, the variability of repeated measures of an object. It is not a measure of how close the estimates are to physical reality: that is termed *accuracy*. A reliable but inaccurate signal would be of little value in calibrating another system. Calibration involves correction of systematic biases, and for that one would like the most accurate signal: even if it happens to be the less precise. Although accuracy is far harder than precision to measure experimentally, we can speculate on which system may have access to accurate information. For example, vision has no direct access to information about object size: this must be calculated by multiplying the size of the retinal image with the distance of the object, which itself can only be estimated indirectly from multiple cues. It makes intuitive sense to suppose, as Berkeley did in 1710, that haptic information is necessary to calibrate a system that is so heavily reliant on inference and experience. Of course touch does not have information about absolute scale, but does have direct access to body-centered and body-scaled size information, which could be a useful calibration tool. On the other hand, primary visual cortex is tuned specifically to orientation (Hubel & Wiesel, 1968), so orientation (at least with respect to a head-centered reference) can be extracted fairly directly. Most models of visual orientation discrimination are very simple, usually involving a simple ratio of responses of differently tuned neurons of V1 (Kwan & Regan, 1998) without requiring extensive calculation, inference, or learning. This led us to suggest that the haptic system calibrates vision for size judgments (following Berkeley's idea), but vision may calibrate the haptic system for orientation (Burr et al., 2011; Burr & Gori, 2011; Gori et al., 2008; Gori et al., 2010; Gori, Sciutti, Burr, & Sandini, in press).

If the selective dominance in cross-sensory judgments does indeed reflect cross-sensory calibration, it leads to very specific hypotheses: early impairments in vision should impact specifically on haptic-orientation, but not haptic-size discrimination; and conversely, early impairment in haptic experience should impact on visual-size, but not visual-orientation discrimination. We have previously tested and verified the first of these predictions, showing that visually impaired children are selectively poorer at haptic orientation discrimination than the control group, while better on size discrimination tasks (Gori et al., 2010). The only exception was one child who became blind after

having had normal vision for the first three years. The results are also supported in the literature by several studies showing poorer haptic performance for blind people on certain haptic tasks, essentially those requiring a sense of orientation, and suggesting a role of visual experience in acquiring these perceptual aspects (Noordzij, Zuidhoek, & Postma, 2007; Pasqualotto & Newell, 2007; Postma, Zuidhoek, Noordzij, & Kappers, 2008). All these results suggest that vision may serve to *calibrate* the haptic sense of orientation, but not of size.

In the current study we test the complementary prediction: that early deprivation of haptic exploration will impact specifically on visual size, but not orientation discriminations. To test this hypothesis, we chose children and adolescents with movement disorders: a group of diseases and syndromes resulting from genetic disorders, brain lesions or other sometimes unknown causes, affecting the ability to produce and control movement, either of the whole body or specific parts, such as hands, feet, arms and legs, and in some cases face and tongue. These patients show reduced capacity to grasp and manipulate objects haptically, particularly with fine movements, and have great difficulties in reproducing hand gestures. The results of this study show that all eight subjects with early-onset movement disorder showed a selective reduction in visual size, but not visual orientation discriminations, providing strong experimental support for the cross-sensory calibration hypothesis.

2. Methods

For the aim of this study we selected children referred to the Stella Maris Scientific Institute in Pisa in the last six months who corresponded to the following inclusion/exclusion criteria: (i) age at testing ranging: 5–18 years; (ii) mild to severe motor impairment due to movement disorders affecting upper limbs; (iii) mild or no mental retardation, according to a standardized Intelligence Scale; (iv) no visual acuity defects or other significant visual abnormality. The research was approved by the Ethical Committee of the Stella Maris Foundation and parental informed written consent for the study was obtained in all cases.

We measured visual discrimination thresholds for size and orientation discrimination in a group of 9 children with movement disorders (3 with choreo-athetotic movements, 5 with dystonic movements, 1 with tremor) of 5–16 years of age: 8 with early onset (neonatal) and 1 later acquired (3 years). The motor impairment to the upper limbs (see Table S1) was evaluated on a score ranging from 0 (no deficit) to 4 (severe disorder), extrapolated from the Movement Disorder-Childhood Rating Scale (Battini et al., 2008). Four subjects have lesions at thalami and putamen revealed by brain MRI due to perinatal hypoxic-ischemic insults and in 1 subject (GM1) a slowly progressive metabolic disorder (gangliosidosis) has been diagnosed; for the others, defined idiopathic, no cause was found despite extensive genetic and metabolic investigations. The cognitive development of all subjects was evaluated by the Wisc-III scale, yielding an intelligence quotient ranging from normality to very mild mental retardation. No visual disorders were found (except in some cases visual, difficulty to hold gaze on an object while trying to reach for it). For all clinical details see Table S1.

The visual size and orientation discrimination thresholds were measured with the child-friendly technique developed by Gori et al. (2008) (see also Fig. 1(A) and (B)). For the size discrimination task the stimuli were physical blocks of variable height (48 to 62 mm, in 1 mm increments) magnetically clamped to at an appropriate height on the screen (Fig. 1(A) and on-line movie). Two stimuli were presented sequentially in each trial: one stimulus (randomly first or second) was the *standard*, always

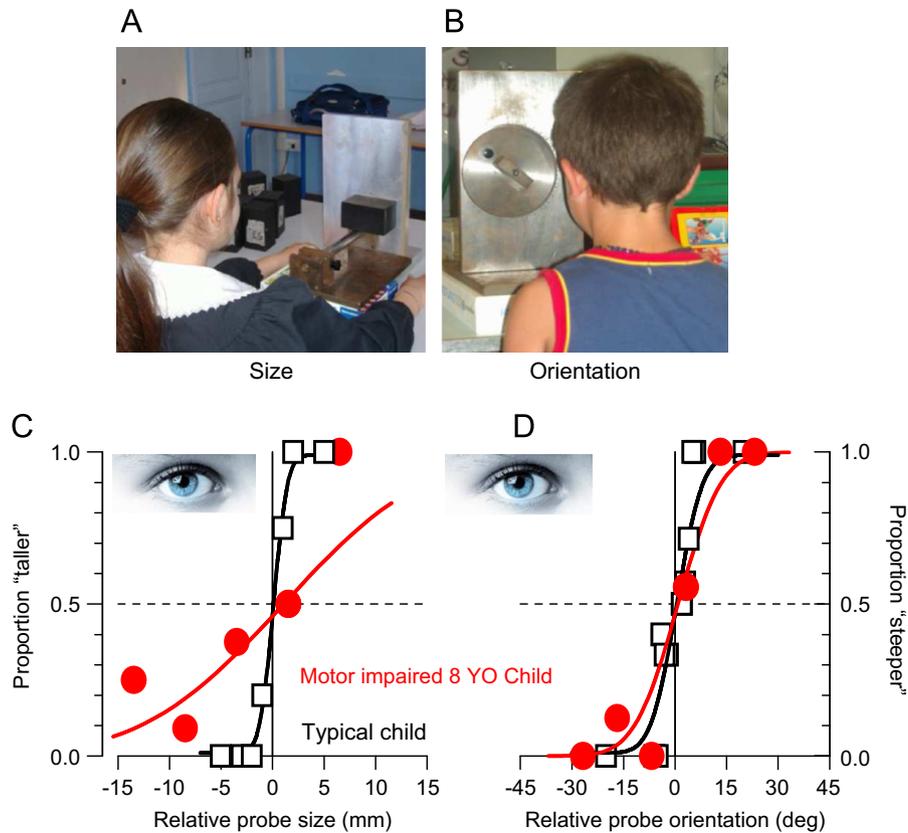


Fig. 1. (A) Setup for the size task. The child observes a sequence of blocks of different height and reports which was higher, (B) setup for the orientation task. The child observes a sequence of two oriented blocks and reports which was more rotated anticlockwise, (C) example of a psychometric function for visual size discrimination, plotting proportion of trials where the test stimulus was judged taller than the standard against of test size (relative to the standard of 55 mm). The data are fitted with a cumulative Gaussian function, whose standard deviation gives an estimate of size discrimination threshold. The curve of the 8-year-old child with movement disorder (subj. 3, filled red circles) is far less steep, producing a threshold 7.8 times higher than the age-matched control (open black squares), (D) same as A, but for orientation discrimination. The psychometric function for the 8-year-old child with movement disorder (filled red circles) is similar to the age-matched control (open black squares).

55 mm high, the other the *probe*, of variable height. Children reported – in forced-choice – which of the two was higher. The procedure for the orientation-discrimination task was similar to that for the size-discrimination, again using a simple, low-technology technique (Fig. 1(B)). Again, two stimuli were presented sequentially in each trial: the *standard* slanted at 45° and the *probe* with variable orientation from 0° to 90°. Children reported which was rotated more counterclockwise. The order of testing of the conditions (orientation and size) was counter-balanced between subjects.

Supplementary material related to this article can be found online at <http://dx.doi.org/10.1016/j.neuropsychologia.2012.04.009>.

The test was presented in the form of a game (see on-line movie for example with typical child). Positioning of the blocks lasted about 2 s, so each trial took around 4 s. Subjects were well trained on the task before collecting data and before the beginning of the test the researcher insured that the child was confident with the concept of size and orientation. To explain the size task young children were shown a very small and a very large block and asked which was larger. For the orientation task, they were asked which of two inclined blocks was more reclined. They were further asked if the block were a slide for a dog on which he would slide faster. For the children with difficulties of vocally reporting their response the researcher associated each temporal interval with a color (for example presenting the first block or orientation together with a red paper and the second with a green paper) and asked to indicate the color associated with the larger or steeper block. Children were seldom bored,

maintaining attention throughout the session. If attention did lapse, the testing was interrupted. The experimenter chatted with the child for a while, and then testing resumed. All trials of a given condition were collected within one session.

The height or orientation of the probe was varied by an adaptive algorithm (Quest: Watson & Pelli, 1983) for a total of about 30–40 trials per condition (depending on the collaboration of each child, as reported in Table S1). The proportion of trials where the probe was judged taller or more slanted than the standard was computed for each probe height and orientation, and fitted with a Cumulative Gaussian function (such as those of Fig. 1(C) and (D)). The space constant (σ) of the fit was taken as the estimate of discrimination threshold for that condition (results in Table S1). The data of the control group were taken from the vision-only condition of our previous study (Gori et al., 2008). For that study 69 children and 6 adults with normal range of IQ were tested.

3. Results

Fig. 1(C) and (D) shows sample psychometric functions for an 8-year-old subject with movement disorder (red symbols) for visual size and orientation discriminations, and an age-matched typically developing child (black symbols). For orientation discriminations, both control and patient performed similarly: the functions are smooth and orderly, and very steep. Orientation discrimination thresholds (standard deviation of the psychometric function) are

$9 \pm 3^\circ$ for the patient and $8.3 \pm 2.1^\circ$ for the typical child. For the size discrimination, however, the psychometric functions were quite different for patient and control: the data for the control are orderly, and fit with a narrow function of standard deviation 1.4 ± 0.3 mm; the data for the patient are quite different, very disorderly, with errors even for size differences as large as 15 mm. The best-fitting curve is very broad, with standard deviation of 11 ± 8 mm.

This pattern of results was observed with every single child with early-onset movement disorder. Fig. 2 plots size (A) and orientation (B) against patient age, with the average thresholds of typically developing children shown for comparison (black curves from Gori et al., 2008). Without a single exception, the thresholds of the patients with early-onset movement disorders (filled red symbols) were worse than the controls of that age, while the orientation thresholds were comparable. We also regressed thresholds against level of motor impairment, but found no significant correlation. No significant difference in precision was observed between subjects with different motor disabilities. It might be argued that the relative deficit on the size task could be associated with the cognitive impairment rather than motor impairment of the test group. However, when the data are replotted in terms of the developmental age derived from IQ testing, the pattern of results from the two tasks, compared to controls, remains the same (Figs. S1, S2 and Table S1).

Fig. 3(A) plots age-normalized size thresholds against orientation thresholds. All data for patients with early-onset movement disorders scatter around the ordinate, with age-normalized orientation thresholds near unity, but size thresholds far greater than one (with mental-age matching we found similar results: see caption in Fig. 3(A) and Table S1). The only exception was case 9, a 17-year-old child who acquired movement disorder at the age of 2 years (blue star), who shows thresholds of one for both orientation and size. Fig. 3(B) shows, for comparison, data from blind children for haptic size and orientation discriminations (reproduced with permission from Gori et al., 2010). These show the converse effect: the patients performed worse than controls on the orientation discrimination, but better for size discriminations.

4. Discussion

The present results complement those of Gori et al. (2010) to support the theory that early cross-sensory calibration is fundamental for the normal development of perceptual systems. An earlier study tested and confirmed the prediction that congenitally blind patients

should show compromised haptic orientation, but not size-discrimination (Fig. 3(B)). This prediction was based on the previous study (Gori et al., 2010) showing that in young children, vision dominates haptic in orientation judgments suggesting that vision calibrates haptic orientation discrimination. The current study tested the complementary prediction: patients with abnormal experience in haptic manipulation should show deficits in visual size but not orientation-discrimination (as the developmental results showed that for size discriminations, haptic discrimination dominates visual discrimination). This prediction was confirmed in each of the eight children with congenital motor deficits, without a single exception, suggesting that for patients with movement disorder, not only is their haptic sensitivity and functionality compromised, but that this impacts heavily on their ability to discriminate visual size. This is consistent with the notion that haptic manipulation is necessary to calibrate the visual sensory apparatus in its estimate of size. As with our previous study, we tested one patient who had acquired movement disorder at the age of 2, and showed normal thresholds for both size and orientation, again consistent with the notion that it is early calibration that is necessary.

The evidence for calibration between senses is steadily accumulating, for many modalities, including vision-audition (e.g., Wozny & Shams, 2011), vision and vestibular input (e.g., Zaidel, Turner, & Angelaki, in press), visual-motor coordination (e.g., Brown, Wilson, Goodale, & Gribble, 2007; Burge, Ernst, & Banks, 2008; Cressman & Henriques, 2009). Cross-comparison between senses is clearly a good strategy to establish and to maintain calibration, as each sense has access to different sources of information, differently affected by noise and distortions. As mentioned in the introduction, while both theory and experiment suggest that signal reliability should govern sensory fusion, it is less clear what to expect for cross-calibration. Reliability is a measure of constancy, or *precision*, that does not necessarily correspond to accuracy (closeness to physical reality), which is what is needed for calibration and error-correction. Few studies have attempted to establish the underlying principles of cross-sensory calibration. Ghahramani et al. (1997) reported that calibration of visual and auditory space was determined by reliability (like sensory fusion), but this may have been a specific case, where precision and accuracy happen to be correlated, and not true in general. In a more recent study, Zaidel et al. (in press) showed that a mismatch between visual and vestibular signals will cause each to recalibrate towards each other, but the amount of recalibration does not depend on reliability, but follows a fixed ratio rule independent of reliability. As previous studies in their

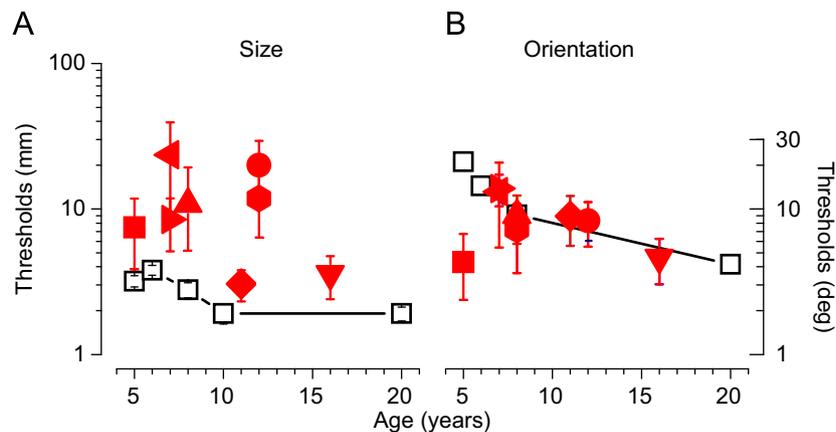


Fig. 2. (A) Size discrimination thresholds for the motor impaired as a function of age. Each red symbol represents a different subject (see Table S1 for more details). Open black symbols show the average of the typical control group taken from (Gori et al., 2008). Error bars on individual data points are ± 1 SEM obtained by bootstrap (Efron, 1993), those on the control data are ± 1 SEM of inter-subject variability, (B) orientation discrimination thresholds for the motor impaired as a function of age, with the same symbol-code as Fig. 2(A).

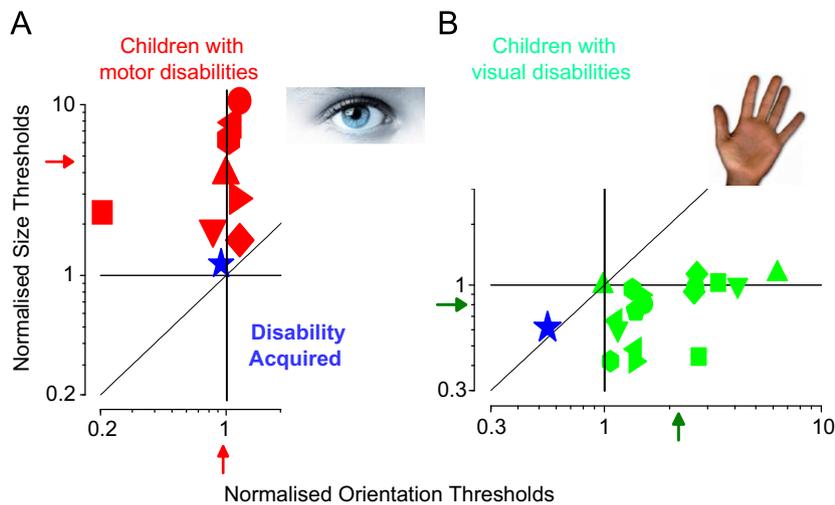


Fig. 3. (A) Individual visual size thresholds of children with motor disabilities normalized by the age-matched controls, plotted against normalized visual orientation thresholds, using the same symbol-code as in Fig. 2(A) & (B). The thresholds were normalized by dividing each value reported in Fig. 2(A) & (B) and Table 1 by the average age-matched control, obtained by interpolating the average thresholds for typical subjects (black lines of Fig. 2(A) & (B)). Most points lie in the upper left quadrant, implying better orientation and poorer size visual discrimination. The red arrows refer to group averages, 0.96 ± 0.12 for orientation and 4.64 ± 1.22 for size. Similar results were obtained with mental-age matching (see Table S1): 0.79 ± 0.18 for orientation and 3.99 ± 0.98 for size. The blue star is the child with later onset movement disorder, (B) individual haptic size thresholds of children with visual disability normalized by the age-matched controls, plotted against normalized haptic orientation thresholds. Most points lie in the lower right quadrant, implying better size and poorer orientation discrimination. The green arrows refer to group averages, 2.2 ± 0.3 for orientation and 0.8 ± 0.06 for size. The blue star in the lower left quadrant is the acquired low-vision child (reproduced with permission from Gori et al., 2010).

laboratory Gu, Angelaki, and Deangelis (2008) have shown that integration of visual and vestibular signals are governed by reliability, this is clear evidence that calibration and fusion can follow different rules.

Young children do not fuse visual and haptic signals, but one or the other dominates: haptic signals for size and vision for orientation. This dominance is not in the direction predicted by reliability as, under the experimental conditions of that study, visual size judgments were more reliable than haptic size judgments, and both were similar for orientation. Reliability – which is a measure of repeatability or precision – is not in general a good criterion for calibration, as it is possible to be reliably wrong. What is needed for calibration is accuracy. Although hard to prove objectively, it makes sense that haptic information may be more accurate than vision for size judgments, as the visual estimate can be made only indirectly, by multiplying retinal size by perceived distance (itself an indirect measure), while visual orientation is encoded in the primary visual cortex. These concepts still require further investigation, but the predictions are clear, and to date very self-consistent.

It is interesting that in this study, like Gori et al. (2010), the one child with an acquired disorder (at the age of two years) showed results that were completely different from the others. Again this is perfectly consistent with cross-sensory calibration hypothesis: this child had had two years of normal haptic behavior, and perhaps this was sufficient to calibrate the visual system for size perception. A similar result was observed in our previous study, where the subject with acquired blindness (at three years of age) showed normal tactile orientation thresholds. We are naturally cautious not to over-interpret the results of one single subject, but they are in line with other evidence suggesting that the first 3 years are fundamental to establish cross-sensory plasticity (Bedny et al., 2010; Morrone, 2010).

Although the concept of cross-sensory calibration is old, dating back to Bishop Berkeley's famous essay (Berkeley, 1709/1963), it has not been extensively studied and remains poorly understood. However, it could be fundamental for patients with severe sensory disabilities, in that not only that sense will be compromised, but

also others that rely on it for calibration. Beyond the theoretical importance of these results, they are obviously also fundamental to understanding fully various sensory losses, and may ultimately lead to new strategies of early rehabilitation.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.neuropsychologia.2012.04.009>.

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