Visuo-motor control in low birth weight children without major ophthalmic or neurologic sequelae

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Abstract

Aim: **To evaluate in a pilot study the use of a touch-screen test in very low birth weight (VLBW) children to explore aspects of visuo-motor behaviour, measuring spatial localisation. Results in VLBW subjects will be compared with those in children born at term. It will be investigated whether any deficits found were related to parental reports of visual function difficulties.**

Methods: **A range of visual functions were measured and IQ estimated using subtests from a standardised test. Using a touch-screen monitor to record pointing positions, in task 1 subjects pointed to sequences of visual targets as soon as they appeared and in task 2 they pointed after a memory delay.**

Results: **Thirty-seven VLBW subjects and 32 control subjects were recruited. On task 1 there was no difference in the pointing error magnitude between the groups. Although the errors of the VLBW group were more variable, this was not statistically significant after exclusion of VLBW subjects with IQ <70. However, on task 2 the VLBW group remembered fewer complete sequences, leading to significantly higher average pointing errors when data were averaged over all sequences. When pointing error was averaged over only correctly remembered sequences, there was again no difference between the groups.**

Conclusions: **Our results indicate that pure spatial localisation in the absence of a memory load in VLBW children is comparable to the performance of children born at term. However, deficits are apparent in VLBW children when working memory is introduced, and this is consistent with the findings of other studies.**

Key words: IQ, Low birth weight, Memory, Spatial localisation, Visual function

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Introduction

Preterm birth is associated with a wide range of complications, some of which result in long-term sequelae,[1] and range from the severely disabling to relatively minor impairments of unknown functional impact. The former can often be predicted from the structural deficits identified[2,3] whereas the latter may be present in the absence of any detectable structural deficit. Recently the focus of research has turned to the very low birth weight (VLBW <1501 g) infant who may be discharged from neonatal care with no identified pathology but who might later exhibit subtle impairments or disabilities. In the visuo-motor domain, these include reduced visual acuity,[4] reduced contrast sensitivity,[5] increased prevalence of strabismus,[6] increased prevalence of all types of refractive errors[7] and specific deficits of eye movement control.[8] In addition to deficits of sensory visual function and oculomotor control it has been shown that VLBW children also have more general visuo-motor difficulties.[9–11] However, clinical assessments often suffer from low sensitivity and involve a qualitative *assessment* of performance rather than a quantitative *measurement* of performance.[9]

Aspects of vision that are measured for routine clinical and management purposes include static visual acuity, contrast sensitivity and colour vision. However, a response that is within normal limits on these tests may not indicate a normally functioning visual system. Given the increased deficits of functional ability related to vision in VLBW children[12] it is of particular importance to fully investigate functional vision. Vision is necessary for many aspects of effective, purposeful behaviour, such as reaching and pointing, yet little is known about these aspects of behaviour in VLBW subjects, even though they are closely related to real-world tasks and therefore to quality of life. The ability to accurately locate objects in visual space and precisely guide the hand to them is important for many real-world functions. The ability to remember positions accurately provides an important degree of behavioural flexibility, allowing actions to be programmed 'off-line' using remembered rather than actual sensory information.

The purpose of this pilot study was to evaluate aspects of visuo-motor behaviour using a touch-screen test in VLBW children. We wished to assess whether spatial

ability, determined by the accuracy of pointing to visual targets, with and without a memory delay, was modified in VLBW subjects (free from major neurological impairments) compared with children born at term, and whether any deficits found were related to parental reports of visual function difficulties.

Methods

Subjects

Procedures were conducted in accordance with the Declaration of Helsinki and were approved by the Liverpool Research Ethics Committee. Subjects were recruited from a single NHS Trust (Aintree Hospital NHS Trust) and were under the continuing care of a single Consultant Ophthalmologist (author D.C.). Parents of eligible children were invited to participate; written consent was obtained from the parent or guardian and written assent was obtained from the subject.

VLBW children were defined as those with a birth weight (BW) of less than 1501 g. Inclusion criteria were: age greater than 8 years and binocular visual acuity (VA) of at least 0.5 logMAR (Snellen equivalent 6/18). Exclusion criteria were: major neurological deficits, cerebral palsy, any known motor disorder that would affect pointing and severe sensory impairments, determined by screening of the hospital records. Details of neonatal health and the severity, extent and treatment of retinopathy of prematurity were obtained from the hospital records. An age-matched control group (matched on a group basis, not by individual) of normal birth weight children (BW >2500 g) with no known neurological defects were recruited from siblings of subjects or children of friends, family or hospital staff.

Tests

Each session lasted no longer than 1 hour. For each subject, the parents or guardians were asked three visual function questions (based on previous clinical reports and Dutton,[13] which describes the impact of cognitive vision disorders) to which yes/no answers were recorded:

1. Does your child have difficulty picking you out of a crowd?
2. Does your child have difficulty with steps and curbs?
3. Does your child have any visual problems in unfamiliar surroundings?

Each subject had a vision assessment (using their current refractive correction where appropriate) consisting of monocular and binocular distance VA (letter logMAR chart, Precision Vision, La Salle, IL), cover test at 1/3 m and 6 m using letter targets to determine the presence of strabismus, and the Bagolini glasses test (performed at 1/3 m and 6 m), to determine whether the subject had binocular single vision. In subjects who demonstrated binocularity with Bagolini glasses, the level of stereo-acuity was measured using the TNO stereo-test (Richmond Products, Albuquerque, NM).

IQ was assessed using a subtest combination from the WISC-III,[14] which is a battery of tests for 6- to 17-year-

olds that evaluates intellectual ability. It consists of two scales, vocabulary and performance (each containing six subtests), which combine to yield the full-scale IQ (FSIQ). A short form of the WISC-III using the Vocabulary and Block-Design subtests can be used as a screening device to identify abnormal IQ[15] as it has been identified as the best combination of subtests,[16,17] having high reliability and yielding a higher correlation with FSIQ than other subtest pairs.[18] The mean score is 100 (SD 15) and a score below 70 (2 standard deviations below the average) is classified as abnormal.

Pointing tasks

Targets were presented on an NEC 20-inch LCD monitor with a capacitive touch-screen controlled by a PC. The touch-screen returned the x and y touch positions. Touch resolution was 4 pixels/mm, and pointing positions and target positions were written to the PC hard disk for offline analysis. Subjects viewed the monitor from 33 cm , with their chin on a rest, and touched the screen with the index finger of their dominant hand (with the other three fingers in a grasp). In each task the targets (black squares on a grey background, subtending approximately 1°) were presented at 1 of 25 randomly chosen positions on a 5×5 grid in sets of 5. Each set of five targets was preceded by an auditory warning signal and followed by a short pause.

Task 1: The subject was instructed to touch the monitor at the target position as soon as each target was presented. In early tests subjects completed 10 trials (i.e. a total of 50 targets); as subject performance was stable across blocks, this was reduced to 5 trials (25 targets).

Task 2: This was identical to task 1 except that subjects had to observe a sequence of five targets, and wait for 5 seconds before touching the monitor at the five target positions, in the same sequence as the targets had been presented, so they had to remember both the sequence and the position of targets within the sequence. A delay of 5 seconds was chosen as there is evidence that after this time the information about location is obtained outwith the visual system and the dorsal visual processing stream.[19] At the end of the 5 second delay an auditory cue and a visual signal indicated subjects should begin pointing. They were not permitted to rehearse target positions; their pointing hand rested on the table until the go signal.

Analysis

The x and y coordinates of the touch points were transformed into polar coordinates, with pointing error recorded as the distance (in pixels) from the centre of the target, and the direction as an angle calculated from 0° (the axis extending vertically upwards, i.e. the y-axis of each target), incrementing clockwise. The directions of the pointing positions were analysed by calculating the number of points in each quadrant (i.e. pointing positions for which the direction of the point relative to the centre of the target fell between 1° and 90°, 91° and 180°, 181° and 270°, or 271° and 360°).

For task 2, in addition to the pointing error for each target, sequences were analysed to determine whether targets were remembered in the correct order. Each

Table 1. Summary age, vision and IQ data for control and VLBW subjects

	Mean ± SD (range)		
	VLBW ($n = 37$)	Control ($n = 32$)	p value (t-test)
Age (years)	12.84 ± 2.78 (8 to 18.75)	12.36 ± 2.75 (9.08 to 19)	0.5
Binocular VA (logMAR)	0.11 ± 0.18 (−0.32 to 0.5)	−0.08 ± 0.1 (−0.32 to 0.12)	<0.001
IQ	77.16 ± 18.84 (48 to 123)	100.63 ± 12.02 (74 to 117)	<0.001

Table 2. Responses to the visual function questions, presented as the number (%) responding 'Yes'

	No. of positive responses to visual function questions			
	0	1	2	3
VLBW	15 (41)	15 (41)	3 (8)	4 (11)
Controls	31 (100)	0	0	0

target and point position was displayed on the 5 × 5 grid sequentially. A correct sequence was a set of 5 targets in which the pointing positions closely matched the pattern of target positions in the sequence. Where sequences were not remembered accurately the first misremembered target was identified, and the whole sequence was marked as misremembered. The proportion of correctly remembered sequences was recorded for each subject and two sets of pointing errors were calculated: the average pointing error for targets from correctly remembered sequences, and the average error for all targets (i.e. including pointing errors from misremembered sequences).

Pointing errors were normally distributed (Kolmogorov-Smirnov test, $p \geqslant 0.1$ in all cases) therefore a t-test was used to compare differences between two groups and ANOVA for multiple comparisons. For comparisons of categorical data, a chi-square test was performed or a Fisher's exact test if more than 20% of the cells had an expected count less than 5. Analysis was both performed on the VLBW group as a whole and repeated after exclusion of VLBW subjects with IQ <70.

Results

Thirty-seven VLBW subjects (23 female) and 32 control subjects (13 female) were recruited between May 2006 and August 2007. The mean age for both groups was 12 years with no statistically significant difference between the groups (Table 1). Binocular VA (with glasses if worn) was lower in the VLBW group compared with the controls, with the poorest VA being 0.5 logMAR (6/18 Snellen equivalent) in the VLBW group ($n = 7$, $\geqslant 0.3$ logMAR) and 0.12 logMAR (6/7.5 Snellen equivalent) in the control group. Fourteen VLBW subjects (38%) had IQ ≤ 70 and 18 (49%) were in the range >70 but <100. There were no control subjects with IQ ≤ 70 and 12 (38%) in the range >70 but <100.

The responses to the three functional questions (Table 2) revealed that more than half of the VLBW group

(compared with none of the control group) responded 'Yes' to at least one of the questions ($\chi^2 = 27.9$, $p < 0.001$) with 57% ($n = 21$) giving a positive response to question 1, 19% ($n = 7$) to question 2 and 27% ($n = 10$) to question 3. Four of the VLBW group (11%) responded 'Yes' to all three questions. There was no statistically significant relationship between the number of questions to which positive responses were given and the level of VA (ANOVA, $F_{3,33} = 1.6$, $p = 0.2$). However, the level of stereo-acuity was statistically significantly related to the number of positive responses (those with no measurable stereo-acuity were coded as 4.0 log units, ANOVA, $F_{3,33} = 4.8$, $p = 0.007$; VLBW: median = 4.0 log units, interquartile range (IQR) = 1.78–4.0; controls: median = 1.78, IQR = 1.0–2.0). Post-hoc analysis demonstrated that the statistically significant difference was between those with one positive response and all the other groups.

Pointing tasks

Task 1

Data from 3 VLBW subjects were lost due to technical difficulties. Fig. 1 shows raw plots of all the pointing positions in each subject for the VLBW and control groups. For task 1 (Fig. 1a, b) we found no statistically significant difference in the magnitude of the mean pointing error (measured in pixels) between the VLBW and control subjects (VLBW (mean ± SD): 28.6 ± 9.9, controls: 29.6 ± 8.3; t-test, df = 65, $t = -0.41$, $p = 0.7$). However, comparison of subjects' coefficient of variation (i.e. the variability in mean pointing error for each subject, averaged across each group) did reveal a statistically significant difference (VLBW (mean ± SD): 21.8 ± 16.4%, controls: 14.5 ± 6.3%; t-test, df = 65, $t = 2.4$, $p = 0.02$). When the analysis was repeated after exclusion of those VLBW subjects with IQ <70 the mean error decreased slightly (to 27.5 ± 9.3 pix); the difference with the control group remained statistically insignificant (t-test $p = 0.3$). However, the coefficient of variation, after exclusion of those with low IQ, was lower (18.0 ± 9.7%) and no longer statistically different from that of the controls (t-test, df = 65, $t = 1.6$, $p = 0.1$).

Analysis of the direction of pointing errors showed that of the whole VLBW group, 20 (59%) had responses in all four quadrants, 9 (27%) had responses limited to three quadrants and 5 (15%) had responses only in two quadrants. In contrast, the control subjects had less variability in their pointing responses: only 10 controls (31%) had responses in all four quadrants, 9 (28%) in three quadrants and 12 (38%) in two quadrants. One had responses limited to one quadrant. As the numbers with responses in only one or two quadrants were small, the responses of those in one, two or three quadrants were combined and compared with those with responses in all four quadrants. Analysis between the groups showed a statistically higher number of responses in all four quadrants in the VLBW cohort ($\chi^2 = 5.06$, $p = 0.03$). After exclusion of the VLBW subjects with IQ <70 the difference failed to reach statistical significance ($\chi^2 = 3.5$, $p = 0.06$).
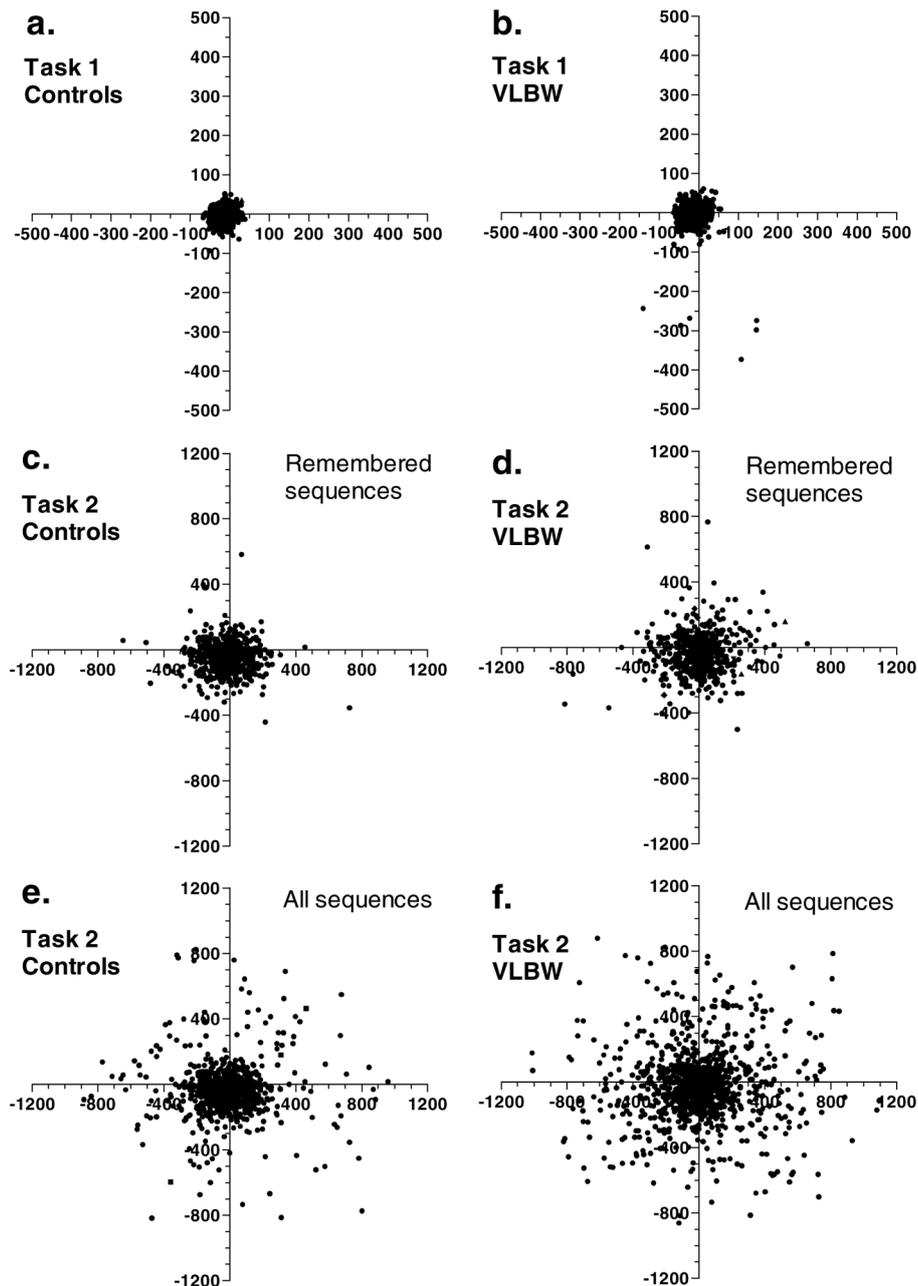
Fig. 1. Data from pointing tasks. Plots show each touch point (in pixels), with all target positions normalised to (0,0). (*a*), (*c*), (*e*) Data from control subjects; (*b*), (*d*), (*f*) VLBW subjects. (*a*), (*b*) Data from task 1. Note the smaller scale. (*c*)–(*f*) Data from task 2 (memory task). (*c*), (*d*) Data from only correctly remembered sequences. (*e*), (*f*) Data from all sequences.

Task 2: memory task

As illustrated in Fig. 1, the magnitude of errors was noticeably higher in the memory task (Fig. 1c–f) compared with task 1 (Fig. 1a, b). Initial analysis of the responses from the memory task included all responses (i.e. both correctly remembered and incorrectly remembered sequences). There was a statistically significant difference in the magnitude of errors (number of pixels) between the VLBW and control groups (VLBW: 271.5 ± 102.2, controls: 184.5 ± 69.7; *t*-test, df $= 64$, $t = 4.0$, $p < 0.001$). However, the coefficient of variation was very similar between the two groups

(VLBW: $41.6 \pm 18.4\%$, controls: $42.9 \pm 20.9\%$; df $= 64$, $t = -0.26$, $p = 0.8$). The same pattern of significantly increased error magnitude in the VLBW group and no difference in the coefficient of variation remained after exclusion of those VLBW subjects with IQ <70. The proportion of correctly remembered sequences was also statistically significantly lower in the VLBW group (49%) compared with the control group (70%; *t*-test, df $= 62$, $t = -2.96$, $p = 0.004$); however, after exclusion of the VLBW subjects with IQ <70 the proportion, while still lower at 57%, was no longer significant (*t*-test, $p = 0.09$).

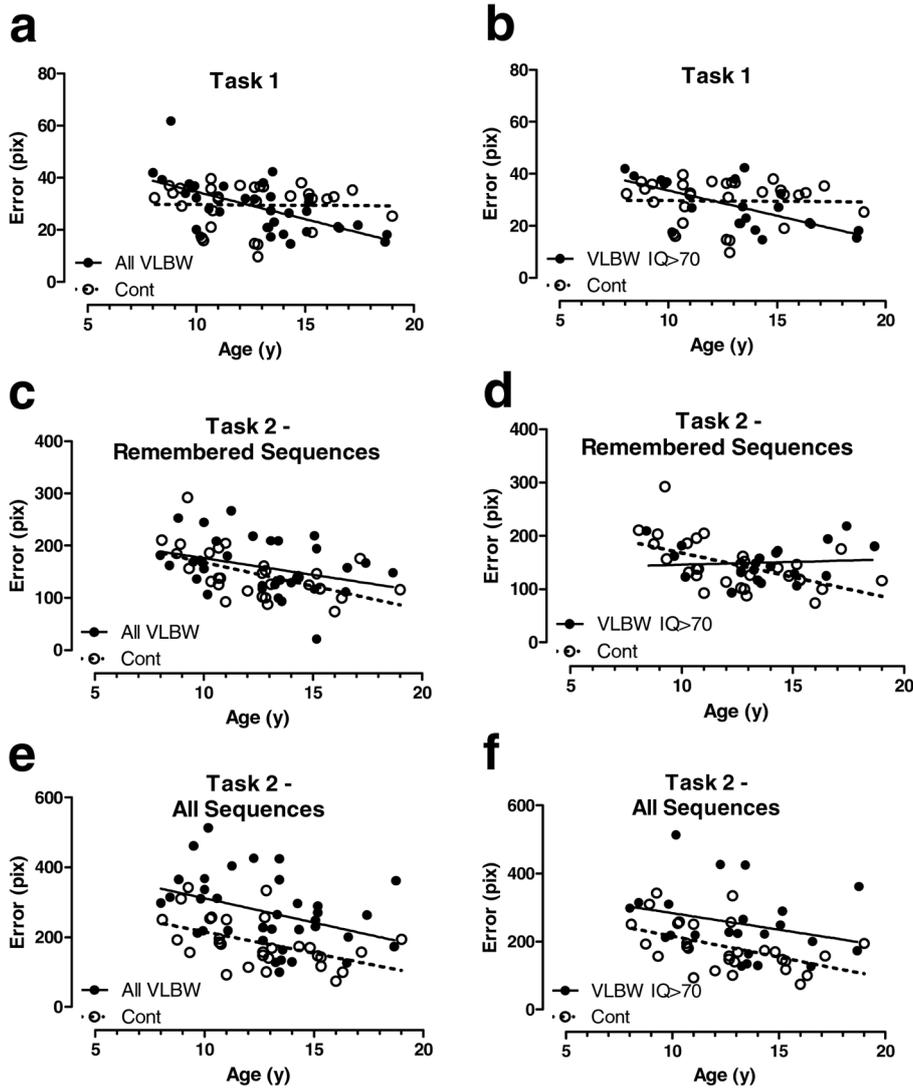When the analysis was repeated for correctly remem-

Fig. 2. Pointing errors (in pixels) plotted against age for the VLBW and control groups. (*a*), (*c*), (*e*) All subjects. (*b*), (*d*), (*f*) After exclusion of the VLBW subjects with IQ <70. Lines are least squares linear regression lines. (*a*), (*b*) Task 1. (*c*)–(*f*) Task 2.

bered sequences only, the error magnitude decreased compared with the analysis of all sequences. While it remained slightly higher in the VLBW group, the difference with controls was not statistically significant (VLBW: 159.2 ± 51.2, controls: 145.4 ± 46.2; *t*-test $p = 0.3$). The coefficient of variation was not statistically different between the groups (VLBW: 29.7 ± 18.2, controls: 24.6 ± 9.9; *t*-test, df $= 62$, $t = 1.13$, $p = 0.2$). After exclusion of VLBW subjects with IQ <70, there was a slight reduction in the VLBW error magnitude (on average 10 pixels), with no difference between groups ($p = 0.7$). There was no difference in the direction of errors between groups either for all trials or for correctly remembered sequences.

Age and pointing error

In task 1 the magnitude of average pointing error did not vary with age within the control group (slope $= -0.056 \pm 0.578$, $r^2 = 0.0003$, $p = 0.9$; Fig. 2a, dotted line). However, there was a statistically significant decrease in the error magnitude with increasing age in the VLBW group (slope $= -2.1 \pm 0.5$, $r^2 = 0.365$, $p = 0.001$; Fig. 2a, unbroken line). This remained when the VLBW subjects with IQ <70 were removed (slope $= -1.9 \pm 0.5$, $r^2 = 0.41$, $p = 0.002$; Fig. 2 d, f). For task 2, analysis of correctly remembered sequences (Fig. 2c) suggested that the error magnitude fell with increasing age in both VLBW (slope $= -6.4 \pm 3.1$, $r^2 = 0.11$, $p = 0.05$) and control (slope $= -9.1 \pm 2.7$, $r^2 = 0.29$, $p = 0.002$) groups. This time, removal of the low IQ VLBW subjects reduced the slope, which was no longer significant (slope $= 1 \pm 3$, $r^2 = 0.01$, $p = 0.7$). When the pointing error calculated from all sequences was included in the analysis (Fig. 2e, f), the error magnitude remained higher across the age range in the VLBW cohort compared with the control group. Error magnitude declined with age for both the VLBW (slope $= -13.9 \pm 5.7$, $r^2 = 0.15$, $p = 0.02$) and control (slope $= -12.3 \pm 4.2$, $r^2 = 0.23$, $p = 0.007$) groups, and

this pattern remained after the low IQ group was removed, although the correlation was no longer statistically significant (slope $= -9.7 \pm 7.3$, $r^2 = 0.1$, $p = 0.2$).

Pointing errors and the functional question responses

For task 1, within the VLBW cohort no statistically significant difference was found in the pointing error magnitude between the group who answered 'No' to all questions (task 1 mean pointing error 29.55 ± 9.25 pix), or 'Yes' to one ($29.0\,8 \pm 11.66$ pix), two (29.97 ± 7.82 pix) or three questions (22.81 ± 8.25 pix; tested with ANOVA, $F_{3,63} = 0.67$; $p = 0.6$). The same was true for the coefficient of variation and the question responses (ANOVA, $p = 0.4$). On task 2 there was a similar lack of association for both correctly remembered sequences and all sequences.

Discussion

The survival of VLBW infants is increasing,[20] raising issues of long-term functional outcome. We compared visual function in a group of VLBW subjects (free from major neurological impairment) with that of an age-matched normal birth weight group. A limitation of this study is that we used a convenience sample from an ophthalmic database. Most of the subjects were not receiving active treatment and were on the database as a result of their VLBW status. However, this was a pilot study to determine whether the tests showed any significant deficit in a VLBW population and to indicate whether the test was related to any functional deficits; these aims could be achieved with this sample of children. Another limitation of this study was the heterogeneous nature of the VLBW group, with a proportion whose IQ was below 70. Although this is reflective of the clinical population, it creates difficulties in the interpretation of the results. If a large sample had been tested with only children with IQ greater than 70 it is possible that some of the analyses may have reached statistical significance.

Static visual measures do not capture many aspects of visual function and the responses of the VLBW group to three simple functional questions revealed that there were clearly perceived problems in the visual domain, as suggested by other reports in the literature.[13] The reduction in stereo-acuity was associated with a positive response to one or more questions, but it is unclear whether this is an association or causal relationship. Although high-grade stereo-acuity is beneficial when performing fine motor skill tasks,[21] there is little evidence to show that a high level of stereo-acuity is required for gross motor skills, particularly in subjects in whom the reduction in stereo-acuity is long term.[22]

In task 1 the performance of VLBW subjects and controls was comparable in terms of error magnitude, but the error direction was more variable in the VLBW group. At present it is unclear whether error magnitude or direction is likely to have the greater functional impact. This increased variability in the VLBW group was driven by those subjects with an IQ <70. Reduced IQ is a frequent finding in VLBW children, although our VLBW group mean IQ is lower compared with what has

been reported in some other studies;[23,24] only 38% of our VLBW group had an IQ <70. As we used the subtest IQ score, rather than the full-scale IQ, we have not sought to draw extensive conclusions about the effect of IQ. Rather than reject the data from these subjects, we have shown that their impact on the overall results was to increase the variability, with the coefficient of variation on task 1 in particular being statistically significantly different from the controls when all VLBW subjects were included in the analysis. After exclusion of those with IQ <70 the difference was no longer significant.

There were differences between the VLBW and control groups in the memory task (task 2) related to remembering sequences. This is consistent with previous reports in VLBW subjects. Short-term working memory deficits have been reported previously.[25,26] Hard *et al.*[27] demonstrated reduced performance on tests of visual perception (including subtests of memory and sequential memory) in a group of preterm infants. However, they did not identify whether any individual component of the test was more affected. In addition, their subjects had a wider range of visual impairment than did our VLBW subjects, where a third had acuities below 0.3 logMAR with the worst being 0.7, and 50% had strabismus.

With previously reported deficits of visual perception in young children (for example the deficits in finding the target in a complex visual search task at 6 years old[28]) it was not possible to determine whether the deficit was a delay in normal development or absolute. In this study the only result that showed a statistically significant association with age was task 1 for the VLBW group, where the error magnitude decreased with age. The r value of 0.6 demonstrated a large effect size[29] with an r^2 value of 0.365, indicating a different pattern of development in the VLBW group. However, for the memory task, when we examined pointing error for all sequences, the data were again consistent with a trend of reducing error magnitude with age in both groups. Across the age range tested, the control group exhibited consistently smaller average errors.

We found no statistically significant associations between the question responses and the pointing tasks, suggesting that the particular tasks used here are not related to the functional problems observed by parents and carers, or that the questions used were not sensitive to the deficits found on the pointing tasks. After the design of this study an inventory for cerebral visual impairment was published[30] with the questions related to a detailed visual assessment. Further testing will use this new tool.

There are two cortical visual processing streams: dorsal and ventral. It has been suggested on the basis of deficits in motion-defined form processing[31] and visual evoked potentials[32] that dorsal stream function[13] is particularly impaired in extremely low birth weight and preterm children. However, the main deficit found here was in relation to memory function (which is where we found deficits in the VLBW group), particularly when related to visually guided actions, which is a ventral stream function. The VLBW group were screened for serious IQ deficits but it is recognised that we cannot rule out the possibility of a role of attentional deficits in this group on this task.

There is published evidence of impairment in a number of domains in the VLBW population as a whole[33,34] but there is a paucity of data examining the subgroup that have either mild or no diagnosed impairments.[35] The findings from this pilot study reinforce previous reports of impaired visual working memory in VLBW children, but suggest generally good performance on low-level sensory and motor aspects of the tasks used. The pointing tasks were feasible in this population but did not show significant deficits alone, therefore further testing of a larger group of children will incorporate other more cognitive aspects of pointing (e.g. spatial localisation with competing distracters or under time constraints), to determine whether they are more sensitive to the functional deficits in this increasing population.

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