Head Growth and Neurocognitive Outcomes

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abstract

BACKGROUND AND OBJECTIVES: There is a lack of evidence on the value of head circumference (HC) as a screening measure. We aimed to describe the incidence of head centile shifting and the relationship between extremes of head size and later neurodevelopmental problems in the Avon Longitudinal Study of Parents and Children.

METHODS: HC was measured routinely at 2, 9, and 18 or 24 months and by researchers at ages 4, 8, 12, and 18 months. IQ according to the Wechsler Intelligence Scale for Children was measured in research clinics at age 8 for all. Neurocognitive disorders (NCDs) were identified from chart review.

RESULTS: There were 10 851 children with ≥2 head measurements. At each age, 2% to 3% of children had scores that were < -2 or >2 SDs below or above the mean, but for most children this was only found at 1 age. More than 15% of children showed centile shifts, but less than one-third of these were sustained at subsequent measurements. Only 0.5% showed a sustained shift beyond the normal range. Children with consistently small heads were up to 7 times more likely to have an NCD, but 85% of children with small heads had no NCDs, and 93% of children with NCDs had head SD scores within the normal range.

CONCLUSIONS: Centile shifts within the normal range occur commonly and seem mainly to reflect measurement error. This finding makes robust assessment of the head trajectory difficult and may result in many children being investigated unnecessarily. Extreme head size is neither specific nor sensitive for detecting NCDs, suggesting that routine measurement of HC is unhelpful.

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Dr Wright conceptualized and undertook this analysis and drafted the manuscript; Dr Emond led the retrospective notes review and planned the data linkage process, negotiated the release of the data, helped plan the analysis, and edited the manuscript; and both authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Microcephaly is known to be associated with neurocognitive disorders and increasing head size with hydrocephalus. Head circumference is widely measured in childhood, but its practical value as a screening test is unclear.

WHAT THIS STUDY ADDS: Measured head size is not a stable characteristic and centile shifts occur very commonly, mostly reflecting measurement error or regression to the mean. Even where head size was consistently extreme, it was not a good predictor of later developmental problems.

The measurement of head circumference (HC) is routinely undertaken as part of the assessment of neurodevelopmental concerns, and it is widely assumed to be a useful clinical tool. The American Academy of Pediatrics (http://brightfutures.aap.org) recommends HC measurement and plotting as part of the complete physical examination 8 times in the first 2 years. In contrast, in the UK, measurement of HC is recommended only after birth and at 8 weeks due to a lack of positive evidence for its usefulness thereafter.[1]

Quality research on the use of HC has been very limited until now. Various developmental conditions are associated with micro- and (rarely) macrocephaly, but a recent clinical review suggested that it is only more extreme microcephaly that is usefully predictive of NCD.[2] One UK study examined children who were referred with HCs crossing below the second UK 1990 percentile. They found that 60% had no identifiable pathology,[3] although this low rate of pathology at least partly reflected the tendency for all children to show a decline on the earlier UK 1990 charts.[4]

HC is also commonly measured as part of surveillance of healthy infants, and thus constitutes a form of screening. Probably the most important pathology potentially identifiable by screening HC is hydrocephalus. A Norwegian study[5] showed the importance of enlarging head size in the diagnosis of hydrocephalus and suggested a prevalence of 7 per 10 000 births, but it is not known how large an increase is usually seen in these children or how many other children show increases without underlying pathology.

The UK adopted the World Health Organization (WHO) HC standard in 2009 along with the WHO standards for weight and height. Although the weight and length/height standards underwent a detailed risk analysis before adoption,[6] the HC standard was published later[7] and so was not appraised. Since then it has become evident that European infants' heads are very large compared with the WHO standards,[4,8] but these large discrepancies are not widely recognized and do not seem to have resulted in strikingly higher rates of referral, suggesting that HC is not in fact widely used to make clinical decisions.

We thus set out to seek new evidence for the usefulness of HC as a screening test. Data from a large UK prospective population-based cohort study provided the opportunity to describe the incidence of extreme head size and head centile shifting and to investigate how this related to later neurodevelopmental problems.

METHODS

The Avon Longitudinal Study of Parents and Children (ALSPAC) is an ongoing population-based study investigating the health and development of children and young people. In 1991–1992, pregnant women who were resident in the former Avon Health Authority in southwest England were enrolled, resulting in a cohort of 15 247 pregnancies and 14 701 children who were alive at 12 months.[9] The study Web site (http://www.bristol.ac.uk/alspac) contains details of all of the data that are available through a fully searchable data dictionary. Ethical approval for the study was obtained from the ALSPAC Law and Ethics Committee and local research ethics committees.

All of the children in the cohort received routine child surveillance examinations by local health services, with HC measured routinely by health visitors (children's public health nurses) at 2, 9, and either 18 or 24 months, depending on the district of residence. These measurements were entered into the local child health computer and were subsequently retrieved for use by the study.

A subset of 1432 of these children (Children in Focus subsample) also had their heads measured by research staff at ages 4, 8, 12, and 18 months. The staff measured heads using a nonelastic plastic tape around the maximum diameter of the forehead and occiput, with the tape wrapped around the head firmly but not drawn tight. Staff were advised to take 3 measurements and to record the highest value.

From the age of 7 years children were called to annual research clinics where a range of measurements were undertaken. These included completion of a short version of the Wechsler Intelligence Scale for Children, 3rd edition (WISC-III), test[10] measured at age 8. A low IQ was defined as total IQ <70.

Educational records linkage to the Pupil Level Annual Schools Census data set for 2003/2004 were used to identify all children recorded as receiving extra classroom support with a Statement of Special Educational Needs (SSEN) by the age of 11 years. This is a formal process used in the United Kingdom to establish the educational needs of children with severe learning difficulty. All cohort members who had a medical assessment for SSEN were identified from community child health records, and those children in the cohort admitted with a relevant developmental disorder were identified from linked hospital admission statistics. A retrospective notes review for all of these children was then undertaken by a team of researchers led by an experienced developmental pediatrician (A.E.) to allocate neurodevelopmental diagnostic International Classification of Diseases, 10th Revision, codes as follows: learning disability (classified as mild or moderate/severe); specific deficits of speech, learning, or motor function; or autism, epilepsy, hyperkinetic disorders, and conduct disorders. Further details of the process used to identify

neurodevelopmental cases in ALSPAC can be found elsewhere.[11]

There were only 2 known cases of hydrocephalus in the cohort, and these cases could not be identified to researchers due to the ALSPAC confidentiality policy concerning rare conditions.

Analysis

All head measurements were converted into *z* scores compared with the WHO growth standard.[12] For each measurement, outliers (>6 and < −6 *z*) were excluded as well as those measurements collected at ages outside the age limits (see Table 1). These *z* scores were then standardized by subtracting the population mean to yield internally standardized scores with a mean (SD) *z* score of 0 (1) at all ages. A summary infancy head *z* score was calculated for each child by using the average of the internally standardized SD scores at 8 weeks and 9 months plus the 18- or 24-month value where available.

Extreme head size was defined as head size below the second (−2 *z*) or above the 98th (+2 *z*) centile. Head size shift was determined by calculating the change in *z* score between 2 and 9 months (early) and between 9 and 18 or 24 months (late). Obvious outliers with shifts between measures of <5 *z* and >5 *z* were excluded. A sustained shift was then defined as a shift of ≥1 *z* in 1 interval with no net recovery in the next interval. Statistical analysis was undertaken by using the Statistical Package for the Social Sciences, version 21 (IBM SPSS Statistics, IBM Corporation, Armonk, NY).

RESULTS

The number of measurements for the total cohort varied from 12 087 at age 6 to 8 weeks to 7077 at age 18 or 24 months; 9279 children had 2 to 3 head measurements, 5378 of whom had all 3 measurements. As described previously,[4] the mean *z* scores compared with the WHO standards were already just above the 75th centile at age 6 to 8 weeks and increased to between the 75th and 91st centiles by age 9 months (Table 1). This mismatch to the WHO standard meant that <1% were below the second centile at any age but up to 18% were above the 98th centile. By using the internally standardized *z* scores, between 2% and 3% were outside either threshold at each age, but three-fourths were only outside this threshold at 1 age (Table2).

In the research subset (*n* = 1312), similar proportions were outside the extreme thresholds at each age. Slightly more children had consistently extreme measures, but two-thirds were still extreme on only 1 measure (Table 3).

Centile shifts were very common in the main data set. By using the WHO standard, upward shifts were much more common than downward shifts between 2 and 9 months. By using the internally standardized *z* scores, similar proportions shifted up and down; >20% crossed >1 *z* upward or downward between 6 to 8 weeks and 9 months and ∼15% crossed >1 *z* upward or downward between 9 and 18 or 24 months. However, approximately three-fourths with shifts between 2 and 9 months showed at least some recovery in the period up to 18 or 24 months and <0.5% showed a sustained shift to outside either the 98th or second centile (Table 2). In the research subset, centile shifts were much less common but still only approximately half of these were sustained shifts. As in the main set, shifts to outside either the 98th or second centile were rare (Table3). By using the internally standardized *z* score (mean = 0.01; SD = 0.88) in the main data set, 2.6% had summary infancy head *z* scores outside either the 98th or second centile.

Neurodevelopmental problems in the cohort

All of the individual neurodevelopmental diagnoses were rare, but of all the children with 2 to 3 head measurements 4.5% had some sort of neurocognitive disorder (NCD; ie, ≥1 neurodevelopmental diagnosis, an SSEN by age 11, or a low WISC IQ). Children with low summary head *z* scores had significantly increased risks of any neurodevelopmental diagnosis, a statement of SSEN at age 11, and low WISC IQ, with the largest excess seen for children with SSEN. Children with high average head SD scores only had a significantly increased risk of any neurodevelopmental diagnosis or of low IQ but no increased risk of an SSEN (Table 4). However, 85% of children with small average head *z* scores and 91% of those with large average head *z* scores did not have an NCD, whereas 93% children with NCDs had head *z* scores within the normal range (Table 4).

For the smaller subset of children measured in the research clinic, the proportion overall with NCDs was similar, although the absolute numbers were small (Table 5). In this subset, a much stronger association between small head size and NCDs was seen but there was no trend to an association with large heads. Nonetheless, ∼90% of children with NCDs had normal-sized heads and

TABLE 1 Number, Age Range, and Mean Values for Routinely Collected HC Measurements From the Main Data Set at Different Ages

Target Age	Number of Valid Measurements	Age, Mean (SD), wk	Age Range, wk	HC, Mean (SD), cm	HC *z* Score, Mean (SD)	Internally Standardized HC *z* Score, Mean (SD)
6–8 Weeks	12 087	7.46 (1.4)	4–12	38.9 (1.4)	0.76 (1.0)	0.00 (1.0)
9 Months	10 343	40.4 (2.9)	27–52	45.8 (1.5)	1.03 (1.0)	0.00 (1.0)
18 or 24 Months	7077	87.7 (11.5)	75–128	48.5 (1.6)	1.05 (1.0)	0.00 (1.0)

TABLE 2 Proportion of All Children in the Main Data Set With Extreme Measurements or Shifts in Head Size

	Number With Valid Measurements	WHO Standard, % (*n*)		Internally Standardized, % (*n*)	
		< −2 *z*	> +2 *z*	< −2 *z*	> +2 *z*
Extreme single measures					
Age					
6–8 Weeks	12 087	0.7 (81)	10.3 (1250)	2.5 (305)	2.3 (277)
9 Months	10 343	0.5 (48)	16.3 (1683)	2.3 (233)	2.9 (304)
18 or 24 Months	7077	0.4 (25)	17.9 (1264)	2.9 (202)	2.6 (186)
Outside threshold (for those with ≥2 head measurements)	10 851				
At 2 ages only		1.1 (116)	14.5 (1574)	4.0 (436)	3.8 (411)
Twice or more		0.1 (7)	9.6 (1046)	0.9 (98)	1.2 (133)
Centile shift >1 *z*		Down	Up	Down	Up
8 Weeks to 9 months	9267	6.6 (611)	18.3 (1694)	11.7 (1085)	11.5 (1066)
9 Months to 18 or 24 months	5909	6.8 (402)	8.3 (492)	7.2 (427)	7.8 (463)
Shift sustained beyond 9 months	5312	1.4 (75)	6.0 (320)	3.0 (158)	3.3 (176)
Early shift to outwith normal range (>2 or < −2 *z*)	9267	0.3 (28)	7.1 (662)	1.1 (102)	1.4 (128)
Early shift to outwith normal range (>2 or < −2 *z*) sustained beyond 9 months	5312	0	2.0 (106)	0.1 (6)	0.3 (16)

between two-thirds and three-fourths of those with small heads had no abnormality. There was no relationship between neurologic abnormality or low IQ with centile shifts in either direction in either the main data set or in the research subset (data not shown).

DISCUSSION

The main findings of this analysis are that although, in principle, head size should be a stable characteristic, in practice it is not, with instances of extreme head size usually occurring in isolation and centile shifts occurring commonly. Even when head size was consistently extreme, this finding was not a good predictor of later developmental problems.

The strengths of this study are that it used a large population-based cohort of healthy children that was generally representative of UK children at the time and HC measures were collected as part of routine health care and were combined with those collected in research clinics. The main limitation is that there were a large number of observers; although all had received training according to a standard protocol for measuring head circumference, no information was available on how compliant the clinicians were in following recognized good practice. However, the health service staff in the Bristol area were probably no better or worse than other clinicians undertaking child health surveillance, so the findings are of relevance to other real-life settings. Missing data were a potential limitation, as in all longitudinal studies, but the very large scale of the cohort meant that there were large numbers for most analyses, and a majority of children were represented in most of the analyses.

These routinely collected HC measurements showed great within-subject variability, suggesting a high degree of measurement error. Even in a research setting, two-thirds of children who were recorded with small heads once were not found to

TABLE 3 Proportion of Children in Research Subset With Extreme Measurements or Shifts in Head Size Using Internally Standardized *z* Scores

	Number With Valid Measurements	< −2 *z*	> +2 *z*
Extreme single measures			
Age			
4 Months	1018	1.9 (19)	2.3 (23)
8 Months	1312	1.1 (15)	2.4 (32)
12 Months	1239	1.9 (23)	2.4 (30)
18 Months	1165	1.5 (17)	1.9 (22)
Outwith threshold (for those with ≥2 head measurements)	1342		
At 1 age only		2.2 (29)	2.5 (33)
Twice or more		1.1 (15)	1.9 (26)
Centile shift >1 *z*		Down	Up
4–8 Months	904	5.2 (47)	3.8 (34)
Sustained shift 4–8 months	901	2.0 (18)	1.6 (14)
Shift at 4–8 months to outwith normal range	904	0.2 (2)	0.6 (5)
8–12 Months	1195	2.7 (32)	2.1 (25)
Shift at 8–12 months to outwith normal range	1195	0.5 (6)	0.4 (5)
Sustained shift at 8–12 months	1183	0.5 (6)	0.5 (6)
12–18 Months	1101	3.7 (41)	3.7 (41)

TABLE 4 Neurodevelopmental Problems in Those in the Main Data Set With 2 to 3 Head Measurements and Relation to Extreme Head Size

Diagnosis	Normal Range	<2nd Centile	P^a	>98th Centile	P^a
All children	97.4 (9034)	1.3 (123)		1.3 (122)	
Learning disability					
Mild	0.6 (56)	4.9 (3)		3.3 (2)	
Moderate/severe	0.2 (18)	5.3 (1)	.005	0	.33
Epilepsy	0.3 (30)	8.6 (3)	.009	5.7 (2)	.07
Autism	0.4 (39)	0	.6	2.5 (1)	.4
Hyperkinetic	0.3 (31)	8.8 (3)	.009	0	.6
Conduct	0.1 (12)	0	.9	0	.85
Specific deficits					
Speech	0.4 (33)	5.6 (2)	.08	2.8 (1)	.37
Learning	0.4 (34)	0	.6	0	.64
Motor	0.1 (6)	0	.9	0	.9
Mixed	0.1 (6)	0	.9	14.3 (1)	.09
Any neurodevelopmental diagnosis	4.1 (367)	9.8 (12)	.005	9.0 (11)	.012
WISC IQ <70[b]	3.4 (166)	10.9 (5)	.021	11.1 (7)	.006
SSEN[c]	2.8 (208)	6.6 (15)	<.001	1.8 (4)	.24
NCD[d]	4.5 (404)	14.8 (18)	<.001	9.0 (11)	.022

Data are presented as % (*n*); *N* = 9279.

[a] Compared with children with heads within the normal range, χ^2 test.

[b] Missing for 4301.

[c] Missing for 1660.

[d] One or more of neurodevelopmental diagnosis, SSEN, or WISC IQ <70.

have small heads again, which suggests that there is a high degree of practically unavoidable measurement error. As a result, apparent shifts in head centiles were frequent, but most were not sustained, with a decrease back to a less extreme centile at the next measurement point.

Probably the most important pathology that is potentially identifiable by increasing HC is hydrocephalus. The Norwegian study[5] described above found that of all children with expansive intracranial pathology, half had been identified on the basis of HC crossing more than "2 percentile curves," 80% of whom had no other symptoms or signs. However, our data suggest that 12% to 18% of children had made a shift of this size, depending on the chart used, with 3% to 6% showing a sustained increase. By using this criterion, to identify the 6 cases per 10 000 children identifiable by screening, at least 1200 children would need to be remeasured and 300 would need more substantial investigation. This level of re-measuring and investigation will create much parental anxiety, unnecessary cranial ultrasounds and CT scans and referral to specialists, solely for reassurance that the child is within the wide range of normal.

Centile shifts in our data occurred most commonly within the normal range, probably reflecting normalization toward the average (regression to mean). Centile shifts beyond the normal range, in contrast, were much rarer and these children may be those who would most merit investigation. What is not known is how large of an increase in HC was usually seen in the Norwegian case series or how many had crossed above the upper centiles, so more research in this area is needed.

TABLE 5 Prevalence of NCDs in the Research Subset by Head Size at Different Ages

	Normal Range	<2nd Centile	P^a	>98th Centile	P^a
4 Months	4.6 (45)	21 (4)	.011	0	.3
8 Months	4.8 (61)	20 (3)	.035	6.3 (2)	.7
12 Months	4.7 (53)	26 (6)	<.001	3.3 (1)	.99
18 Months	4.7 (53)	35 (6)	<.001	4.5 (1)	.99

Data are presented as % (*n*) with later NCDs.

[a] Compared with normal range, Fishers' exact test.

With extreme small head size it is easier to identify a clearly abnormal group, by setting a low threshold (-2 *z*) and rechecking low measurements for consistency. In this data set, only ~1% were consistently below the internally standardized second centile and these children did have up to a sevenfold increased risk of NCDs when measured in a research setting. Nonetheless, the great majority of children with NCDs had heads within the normal range and most children with small heads did not go on to have an NCD. This finding is compatible with a large US study in an unselected population that found that half the children with very small heads (3 *z* below the internally standardized mean) had an IQ <70,[13] but for those with heads between -2 and -3 *z* only 10% had learning difficulties compared with 3% of those with heads within the normal range.

It is of note that we found no association between centile shifts and NCDs. An earlier analysis of the ALSPAC 10% substudy[14] and 1 other study[15] found that head growth during infancy was associated with IQ, but the observed IQ variation in these studies was small and all of the children studied were within the normal range.

When a measure is applied widely to otherwise healthy individuals it constitutes screening and raises the question of how well measurement of HC meets the criteria of a good screening test.[16] On the positive side, HC measurement is quick, cheap, and safe and the conditions of interest are important. Hydrocephalus meets the essential criteria of being treatable, having a latent stage before becoming fully manifest, and benefiting from early identification, but most forms of NCDs do not. However, the key problem is that HC measurement has a high false-positive rate for both possible hydrocephalus and NCDs and a very low sensitivity for NCDs.

CONCLUSIONS

When HC is measured, clinicians and parents can be reassured that the majority of children with small heads will have no underlying pathology and that the commonest explanation for an increase or decrease in head centile is measurement error. Given the great variability in HC measurement, the more often a child's head is measured, the more often spurious extreme or shifting head size will be seen. The implication of this variability is that repeated measurement of HC in infancy is unhelpful and should be undertaken only when an early measurement is outside +2 SDs. The guidelines for the Bright Futures Health Supervision visits recommend a "complete physical exam" including HC measurement at each visit. We suggest an HC measurement in the first 2–5 days after birth, but not in the first 48 hours to allow time for resolution of molding during birth[17] and once more before the age of 6 months. Otherwise, HC should not be routinely measured as part of a complete physical examination, and we suggest that the American Academy of Pediatrics and the Healthy Child Program in the United Kingdom should reconsider their recommendations in the light of this evidence.

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