

Intellectual development at 10 years in early treated congenital hypothyroidism

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Abstract

Fifty nine children born between 1978 and 1981 with congenital hypothyroidism detected by neonatal screening were assessed at 10 years using the Wechsler intelligence scale for children, together with 59 matched classroom controls. Thirty one children with severe hypothyroidism who had pretreatment plasma thyroxine concentrations of 40 nmol/l or less had a mean (SD) full scale IQ score of 104.7 (15.1), compared with a mean (SD) score of 114.6 (16.3) for the 28 less severely affected children who had pretreatment thyroxine levels greater than 40 nmol/l, and mean (SD) scores of 114.5 (12.8) and 114.8 (13.8) respectively for the 31 and 28 control children. In the hypothyroid children the IQ scores at 10 years were closely related to the IQ scores at 5 years and at 3 years. It is concluded that the deficit in IQ score found at 3 and 5 years in children with severe hypothyroidism is still evident at the age of 10 years.

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During the last two decades neonatal screening programmes for congenital hypothyroidism have been set up in most countries with advanced health care systems. Although reports on the psychological outcome in children detected by screening indicate an improvement in outcome, with IQ scores generally within the normal range, a number of studies have reported some deficit in intellectual functioning, but this has not always been of statistical significance.¹⁻⁶ In a pilot study in the UK, a group of children with congenital hypothyroidism born between 1978 and 1981 tested at 3 years on the McCarthy general cognitive index showed an overall deficit of four points compared with controls.⁷ When retested at 5 years using the Wechsler pre-school and primary scale of intelligence (WPPSI) the group showed a deficit of only two points compared with controls.⁸ At both ages, however, the children with severe hypothyroidism (as judged by low pretreatment plasma thyroxine concentrations) did significantly less well than either the less severe cases or the matched controls.

As yet, relatively few studies^{9 10} have reported follow up beyond about 7 years of age. This paper describes our findings at 10 years using the Wechsler intelligence scale for children - revised (WISC-R) in the group of children with congenital hypothyroidism born between 1978 and 1981, many of whom were previously tested at 3 and 5 years of age.

Subjects and methods

SUBJECTS

Details of the group of children born with congenital hypothyroidism in 1978-81 have already been published, together with the results of psychometric assessments at 1, 3, and 5 years of age.^{7 8 11} Of the original sample of 76 patients,¹² six have moved abroad and are lost to follow up, one family refused consent for the study, and one child with congenital cataracts could not complete the test procedure. The remaining 68 children were assessed soon after their tenth birthday. Nine of these children, however, have been excluded from the main statistical analysis; three had additional handicaps (two deaf; one Sotos' syndrome) and were at special schools (IQ scores 59, 59, and 73), four did not have matched controls (IQ scores 109, 109, 120, and 127), and in two patients no pretreatment thyroxine values were available (IQ scores 97 and 113), leaving a study group of 59 children with congenital hypothyroidism and 59 classroom controls matched for age (within three months), sex, social class, and main language spoken at home. These 59 patients did not differ significantly from the 17 excluded patients with respect to pretreatment thyroxine concentration or age at start of treatment.

As previous studies in this group of children had indicated that more severe hypothyroidism was associated with a greater deficit in IQ score, the subjects have been divided into two groups: 31 children with pretreatment thyroxine concentrations of 40 nmol/l or less and 28 children with pretreatment thyroxine concentrations greater than 40 nmol/l; the median age at the start of treatment was 26 days (range 10-40 days) in the first group and 27.5 days (range 19-57 days) in the second.

PSYCHOLOGICAL ASSESSMENT

The children were assessed using the five verbal and five performance subtests of the WISC-R. The tests were carried out in schools by the same psychologist (WFS) who was blind to the results of previous assessments and the pretreatment thyroxine concentrations.

STATISTICAL ANALYSIS

The statistical significance of differences in mean values between the hypothyroid children and controls, and the two groups of hypothyroid children was assessed using *t* tests. The full scale IQ results were also compared with the scores obtained at 3 and 5 years using linear regression and correlation analysis.

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Table 1 Mean (SD) values for WISC-R performance, verbal, and full scale scores in 59 children with congenital hypothyroidism and 59 healthy children matched for sex, age, social background (non-manual/manual), and language spoken at home

	Children with congenital hypothyroidism (n=59)	Control children (n=59)
Verbal IQ	109.6 (16.9)	114.2 (14.0)
Performance IQ	107.4 (15.1)	112.3 (11.7)
Full scale IQ	109.4 (16.3)	114.6 (13.2)

A probability of less than 0.05 was taken to indicate statistical significance.

Results

Table 1 gives the mean verbal, performance, and full scale IQ scores for all the hypothyroid children and their controls. Overall, the mean scores for the hypothyroid children were four to five points below those for the controls, but the differences were not statistically significant.

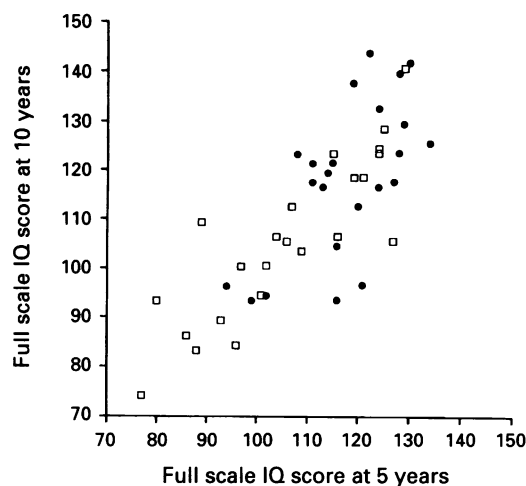
Table 2 gives the mean results for all the WISC-R subtests together with the verbal, performance, and full scale scores for the hypothyroid children divided into two groups by pretreatment thyroxine, and for their controls. The children with severe congenital hypothyroidism (pretreatment thyroxine 40 nmol/l or less) showed a deficit of about 10 IQ points with respect to the verbal, performance, and full scale scores, compared with those with less severe congenital hypothyroidism (pretreatment thyroxine greater than 40 nmol/l) and to the two groups of controls. This deficit in the children with more severe hypothyroidism was present across all the subtests except for picture completion.

Table 3 gives the mean results for the full scale IQ scores for the two groups of children with congenital hypothyroidism, compared with the mean full scale scores previously obtained at 3 and 5 years. At all three ages the differences between the scores for the children with severe congenital hypothyroidism and those less severely affected reach statistical significance (t 2.06–2.93; $p < 0.05$ to < 0.01).

IQ assessments at 10 years showed highly significant correlations with the results obtained at 3 years ($n=48$; $r=0.73$; $p < 0.0001$)

Table 2 Mean (SD) values for the WISC-R subtest scores and the composite performance, verbal, and full scale scores in 31 children with severe hypothyroidism (pretreatment thyroxine 40 nmol/l or less) and 28 children with less severe hypothyroidism (pretreatment thyroxine greater than 40 nmol/l), together with the mean scores for their respective controls

	Pretreatment thyroxine ≤ 40 nmol/l (n=31)		Pretreatment thyroxine > 40 nmol/l (n=28)	
	Patients	Controls	Patients	Controls
WISC-R subtest				
Information	9.1 (3.7)	9.8 (2.7)	10.3 (3.2)	10.4 (3.1)
Similarities	12.3 (3.3)	13.5 (2.9)	14.0 (3.0)	14.3 (2.6)
Arithmetic	9.9 (3.2)	11.9 (2.8)	11.7 (3.6)	11.7 (3.5)
Vocabulary	10.5 (2.6)	11.2 (2.1)	11.8 (2.8)	11.7 (2.1)
Comprehension	12.8 (3.3)	14.2 (2.9)	13.9 (2.8)	14.7 (2.6)
Picture completion	12.3 (2.1)	12.4 (2.4)	12.1 (2.5)	12.0 (1.4)
Picture arrangement	11.1 (2.3)	12.3 (2.9)	12.4 (2.9)	11.3 (3.0)
Block design	11.4 (3.2)	12.3 (2.7)	12.4 (3.8)	11.9 (2.5)
Object assembly	9.7 (3.2)	11.4 (2.6)	11.1 (3.5)	10.7 (2.5)
Coding	7.9 (2.6)	11.3 (2.4)	10.8 (3.3)	12.0 (3.2)
Verbal IQ	105.4 (16.4)	112.8 (13.0)	114.2 (16.5)	115.7 (15.2)
Performance IQ	103.1 (13.3)	113.4 (11.6)	112.0 (15.8)	111.0 (11.9)
Full scale IQ	104.7 (15.1)	114.5 (12.8)	114.6 (16.3)	114.8 (13.8)



Full scale WISC-R IQ scores at 10 years versus full scale WPPSI scores at 5 years in 46 children with congenital hypothyroidism diagnosed by screening. Open squares represent patients with pretreatment thyroxine concentrations of ≤ 40 nmol/l; closed circles represent patients with pretreatment thyroxine concentrations > 40 nmol/l ($r=0.78$).

and at 5 years ($n=46$; $r=0.78$; $p < 0.0001$). The figure shows a plot of IQ scores at 10 years against results obtained at 5 years for the same 46 children.

Discussion

The results of this study show clearly that although the mean IQ scores in children with early treated congenital hypothyroidism generally fall within two standard deviations of the mean for the control population, deficits in IQ scores are consistently present in those children who have more severe forms of hypothyroidism (plasma thyroxine 40 nmol/l or less at diagnosis). This is evident by 3 years of age and persists at 5 and 10 years, and is not compensated for by five years of full time education.

These results are in agreement with the findings in a national cohort of children born between 1982 and 1984 (after the children in the present study) and tested at the age of 5 years. The results showed a non-linear association between pretreatment thyroxine and later intellectual functioning, with a threshold effect at about 43 nmol/l.¹³ Owing to the smaller sample size in the present study, however, the

Table 3 Mean (SD) values for WISC-R full scale scores at 10 years in children with severe hypothyroidism (pretreatment thyroxine 40 nmol/l or less) and less severe hypothyroidism (pretreatment thyroxine greater than 40 nmol/l), together with results previously obtained for the mean full scale WPPSI scores at 5 years and McCarthy (short form) scores at 3 years

	Pretreatment thyroxine concentration	
	≤ 40 nmol/l	> 40 nmol/l
WISC-R: results at 10 years		
No of children tested	31	28
Mean full scale score	104.7 (15.1)	114.6 (16.3)*
WPPSI: results at 5 years		
No of children tested	22	24
Mean full scale score	104.8 (15.3)	116.0 (10.5)†
McCarthy scales (short form): results at 3 years		
No of children tested	26	22
Mean full scale score	96.8 (11.6)	108.5 (17.1)†

* $p < 0.05$; † $p < 0.01$.

data have not been subjected to the same statistical analysis with regard to non-linearity as in the national study. Nevertheless, the present data are entirely consistent with the findings in the larger study.

Most published studies of children with congenital hypothyroidism detected by screening which have examined intellectual development have observed some evidence of intellectual impairment despite early treatment. Small, non-significant IQ deficits compared with controls have been reported in Quebec (four point deficit at 5 years),¹ Switzerland (four point deficit at 4 years),² Toronto (four point IQ deficit at 5 years),³ and France (two point IQ deficit at four years).⁵ Larger statistically significant deficits have been reported in Norway (11 point IQ deficit at 6 years)⁶ and Australia (15 point verbal IQ deficit and six point performance IQ deficit at 5 years).⁴ Some studies have also suggested an association with the severity of the disorder at diagnosis; for example, the Toronto study found a 12 point deficit between severely affected children and those less severely affected.³

The New England Congenital Hypothyroidism Collaborative study is an important exception, finding no intellectual impairment at any age.⁹ Of 72 patients reported at 9 years of age there was a non-significant deficit of three IQ points, with no evidence of academic impairment compared with non-affected peers. No relation between severity of hypothyroidism and outcome was apparent. Differences in the proportion of patients with pretreatment thyroxine concentrations less than the 40 nmol/l threshold might explain the differences between these studies.

These results also show that assessments carried out at 3 and 5 years of age are highly predictive of intellectual functioning at 10 years in children with congenital hypothyroidism. This finding would be expected in normal children and supports the view that the speed of intellectual development in children with congenital hypothyroidism does not

significantly deviate from the expected pattern during the years of primary education.

In conclusion, our findings indicate that at 10 years there is a persistent impairment of IQ score in children with severe congenital hypothyroidism, despite early treatment, and it remains to be seen whether this is associated with educational or behavioural difficulties.

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