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Evaluation of Intellectual Function Associated with Maternal and Pediatric Thyroid Dysfunction

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Abstract

Objective: The purpose of this study was to evaluate the characteristics of intellectual function of children whose mother had thyroid dysfunction, as well as children with hypothyroidism.

Methods: A total of 47 children aged five to seven, who were referred to the center for developmental evaluation at the national child health and development in Tokyo, Japan, were included in this study. The children were divided into two groups: Group A, children with euthyroidism whose mothers had thyroid dysfunction; Group B, children with hypothyroidism. For each group, unpaired t-test was conducted by comparing with the scores of the Japanese version of the Wechsler intelligence scale for children-fourth edition (WISC-IV).

Results: There were 26 children in Group A, 21 in Group B. The scores of Full Scale Intelligence Quotient (FSIQ), Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI), Working Memory Index (WMI) and Processing Speed Index (PSI) by WISC-IV were significantly higher in Group A than Group B (FSIQ, VCI; $P < 0.01$, PRI, WMI, PSI; $P < 0.05$).

Conclusions: There were differences in intellectual function between the children with hypothyroidism and the children who did not have low thyroid hormone level. Low level of thyroid hormone during the neonatal period may be important for intellectual development.

Keywords: Pediatric hypothyroidism; Maternal thyroid dysfunction; WISC-IV

Introduction

Thyroid hormones impact on intelligence, behavior and cognition and are essential for normal development of the central nervous system [1,2]. Studies have suggested that mental retardation is induced in children born from mothers with hypothyroidism [3-5]. In addition, one study reported Attention Deficit Disorder (ADD)-like symptoms in children with asymptomatic hypothyroidism [6]. That study also found panic disorder, depression and disorder add in patients with elevated thyroid stimulating hormone (TSH) levels. In other studies, children with any endocrine disorders, even with euthyroidism, were reported to have the potential for emotional and behavioral problems [7,8], while children with chronic disease are known to be at increased risk of emotional and behavioral problems [9,10].

The Wechsler Intelligence Scale for Children (WISC) was developed in 1949 as an individually administered intelligence test for children, with the fourth version (WISC-IV) released in 2003 [11]. The standardized Japanese version, for use in children aged between ages 5 years to 16 years 11 months, was published in 2012 and has since been used nationwide [12]. Using the WISC-IV, the characteristics of an individual's intellectual development can be comprehensively evaluated based on the scores of the Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI), Working Memory Index (WMI), Processing Speed Index (PSI) and Full Scale Intelligence Quotient (FSIQ).

In Japan, there are few studies that have investigated the relationship between thyroid function of the mother in early pregnancy and fetal brain development. Contrary to studies conducted elsewhere [3-5], a nationwide survey showed that there were hardly any difference among children with congenital hypothyroidism and normal children [13].

Here, we investigated whether intellectual function varies between children whose mothers had thyroid dysfunction and children with and without thyroid dysfunction associated with congenital thyroid disease, using the Japanese version of the WISC-IV.

Subjects and Methods

Subjects

Patients: Participants were children who have received treatment at the department of endocrinology at the National Center for Child Health and Development (NCCHD) in Tokyo, Japan. The children, aged between five and seven years old, were subsequently referred to the center for developmental evaluation between august 2012 and

December 2014 because all of them had either hypothyroidism, or their mothers had thyroid dysfunction.

The children were categorized into two groups: Group A, children with euthyroidism whose mother had thyroid dysfunction; Group B, children with hypothyroidism.

Diagnosis of thyroid dysfunction

The health condition of the mothers and children was diagnosed by maternal healthcare specialists and pediatric endocrinologists. Thyroid dysfunction in mothers included grave's disease or hashimoto's disease. A group of children had gone through newborn screening. Hypothyroidism in Group B children was either permanent congenital hypothyroidism or transient congenital hypothyroidism, and was treated with oral medicine according to the thyroid hormone levels. Children five years or older were examined by a clinical psychologist using the WISC-IV. Patients with secondary hypothyroidism, thyroid dysfunction in both themselves and the mother and other conditions such as birth asphyxia or significantly preterm or chromosomal abnormalities, genetic diseases and intellectual problem, were excluded. Those who were unable to complete the WISC-IV at six years or older were also excluded.

Methods

Using the WISC-IV, we examined whether there were differences in intellectual function between the two groups. As the comparison standard, an average of 100 for the four factors examined and an average of 10 in the subcategories were employed.

Statistical analysis

Stata version 13.0 (Stata corp. collage station, TX) was used for all analyses. Continuous data were compared between two groups by unpaired T-test. For all tests, two-tailed significance values of $P < .01$ or .05 were chosen.

Ethical consideration

Data for this study were collected retrospectively based on medical charts. Publication of this paper was approved by the ethical committee of the national center for child health and development.

Results

Patient attributes

The clinical characteristics of two groups are shown in Table 1. A total of 47 patients (27 males, 20 females; average month of age, 73.37 months, sd 5.6) were included in the study. Details were as follows: Group A, 26 cases (hashimoto's disease, 17; basedow's disease, 9); Group B, 21 cases. The average age of children in Group A; 75.19 months (sd 4.9) was significant higher than that of Group B; 71.33 months (sd 6.1). There were no significant differences between Group A and b with gestational age ($p > 0.05$) and birth weight ($p > 0.05$).

Table 1 shows the clinical characteristics of the all groups. The average age of children in group was significant higher than that of Group B. There were no significant differences between both groups with gestational age, and birth weight.

	Group A N = 26		Group B N = 21		p
At evaluation					
Months of age, (Month), SD	75.19	4.9	71.33	6.1	0.023*
Females (%)	10	38.5	11	52.3	
At birth time					
Gestational age (WK), SD	38.9	1.09	39.00	1.40	0.938
Birth weight (g), SD	3008	340	2856	397	0.172
Passed of mass-screening (%)	26	100	0	0	
T test P < 0.05*					

Table 1: The clinical characteristics; Group A: Children with euthyroidism whose mother had thyroid dysfunction; Group B: Children with hypothyroidism.

Results of WISC-IV

Figure 1 and Table 2 shows the results of the WISC-IV in two groups. There were significant differences between Group A and Group B in FSIQ (P = 0.004), VCI (P = 0.006), PRI (P = 0.024), WMI (P = 0.010) and PSI (P = 0.034) (Unpaired T-test). In both groups, the mean score of results were: FSIQ > WMI, VCI > WMI, PRI > WMI, PSI > WMI of the four factors, the score of WMI exhibited the lowest however, there were no significant discrepancy in VCI-WMI, PRI-WMI and PSI-WMI between two groups.

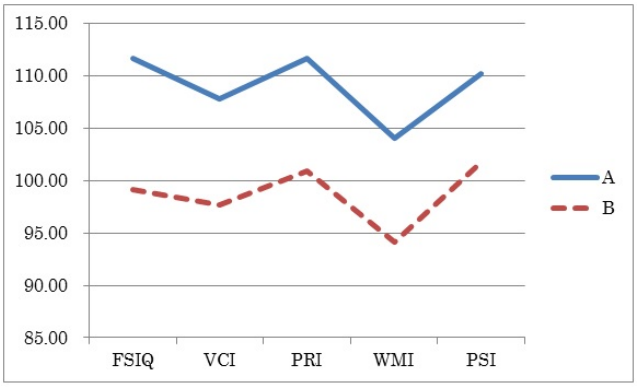

Figure 1: Characteristics of WISC-IV index in both groups; Group A: Children with euthyroidism whose mother had thyroid dysfunction; Group B: Children with hypothyroidism.

Figure 1 shows the mean scores of the WISC-IV in both groups. In both groups, the mean score of results were: FSIQ > WMI, VCI > WMI, PRI > WMI, PSI > WMI of the four factors, the score of WMI exhibited the lowest.

Table 2 shows the results of the WISC-IV in the all groups. There were significant differences between Group A and Group B in FSIQ (P

= 0.004), VCI (P = 0.006), PRI (P = 0.024), WMI (P = 0.010) and PSI (P = 0.034) (Unpaired T-Test).

	Group A (N = 26)	Group B (N = 21)	Comparison between A and B
FSIQ	112.65	99.1	p = 0.004**
SD	18.25	10.55	
VCI	109.04	97.71	p = 0.006**
SD	15.07	11.78	
PRI	112.04	100.95	p = 0.024*
SD	19.22	13.24	
WMI	105.65	94.14	p = 0.010*
SD	17.01	11.00	
PSI	109.89	101.76	p = 0.034*
SD	14.59	10.79	
T test P < 0.05* T test P < 0.01 **			

Table 2: The result of WISC-IV; Group A: Children with euthyroidism whose mother had thyroid dysfunction; Group B: Children with hypothyroidism.

Discussion

To date, there are several studies about maternal thyroid dysfunction and intellectual development of children [14-17], congenital hypothyroidism and their intellectual aspect [18,19] and subclinical thyroid disorders and cognitive functions [20]. However, this is the first pilot study in Japan that compares the intellectual function among children with various background of thyroid dysfunction.

We found that all the indices in Group A were significantly higher than in Group B were observed. We think that the reduced intelligence in Group B was largely due to the children's own hypothyroidism rather than from maternal thyroid dysfunction. There were differences of intellectual function between Group B children with hypothyroidism even if they had treatment and Group A children who did not have low level of thyroid hormone. We postulate that a low level of thyroid hormone during the neonatal period is important for intelligence development.

Although most of the mothers in this study had hypothyroidism, there were also hyperthyroidism cases in Group A. Hence, further study is necessary to investigate children with different background in maternal thyroid diseases.

In Japan, due to the nationwide mass screening of congenital disorders, IQ in children with hypothyroidism is generally not lower than normal because of the early treatment intervention [13,21,22]. Oerbeck et al. reported long-term cognitive deficits in young adults with congenital hypothyroidism relative to control subjects. Verbal and arithmetic functions were associated with l-thyroxin treatment variables, suggesting that more optimal treatment could be possible [19]. A possible reason for the relatively high FSIQ in Group B is that all of the children received some form of treatment for hypothyroidism during the neonatal or infantile period.

Several limitations of this study should be mentioned. First, this study was performed at a single institution. Hence, there might have been a bias in case selection. Second, in Group A children, were not lower than congenital hypothyroid screening level at their neonatal period, the level of thyroid hormone at infancy period is not clear. Furthermore, we did not have a control group whose socioeconomic status of the parents matched with the mothers in the study group. Also, it is noteworthy that the Japanese version of WISC-IV was used. Hence, it is necessary to have a control Group and to increase the number of cases with various socioeconomic backgrounds.

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