sciendo

ENDOCRINE REGULATIONS, Vol. 58, No. 4, 259–265, 2024

doi:10.2478/enr-2024-0031

The relationship between serum thyroid hormone levels and symptoms severity in young children with autism

Maria Kopcikova [1], Barbara Raskova [1], Ivan Belica [1], Jan Bakos [1,5], Hana Celusakova [2], Zuzana Chladna [3], Jana Zibolenova [4], Daniela Ostatnikova [1]

[1]Faculty of Medicine, Institute of Physiology, Comenius University, Bratislava, Slovakia; [2]Faculty of Arts, Department of Psychology, Comenius University, Bratislava, Slovakia; [3]Faculty of Mathematics, Physics and Informatics, Comenius University, Bratislava, Slovakia; [4]Jessenius Faculty of Medicine, Comenius University, Martin, Slovakia; [5]Institute of Experimental Endocrinology, Biomedical Research Center, Slovak Academy of Sciences, Bratislava, Slovakia
E-mail: Kopcikova7@uniba.sk

Objective. Autism spectrum disorders (ASD) are neurodevelopmental disorders characterized by impaired social interaction and communication, restrictive and repetitive patterns of behavior, interests and activities. The aim of this study was to determine the postnatal levels of thyroid hormones and investigate their association with the severity of ASD symptoms.

Methods. The study included 56 children (46 boys and 10 girls) with ASD aged 24–42 months. For ASD diagnostics the Autism Diagnostic Observation Schedule - second version (ADOS-2) and the Autism Diagnostic Interview-Revised (ADI-R) – interview with the child's parents or guardians were used. Venous blood was drawn right after the diagnostic procedures to analyze serum thyroid-stimulating hormone (s-TSH), free triiodothyronine (s-fT3), and free thyroxine (s-fT4) levels. Linear regression analysis was conducted to assess the relationship between the concentrations of thyroid hormones and ASD symptoms severity.

Results. Serum concentrations of measured hormones were within normal reference ranges in almost all children. Decline of s-TSH was significantly associated with an increase in the severity of impaired social interaction and impaired communication as rated by parents (ADI-R) and with a higher prevalence of stereotyped behavior as observed in the diagnostic examination (ADOS-2). A decrease in s-fT3 was associated with higher frequency of stereotyped behavior as assessed by parents (ADI-R). Neither sex nor age were significant predictors.

Conclusion. Although thyroid hormone levels were normal, we demonstrated an association of thyroid hormones with ASD symptoms.

Keywords: Autism spectrum disorder, children, serum, thyroid hormones

Autism spectrum disorders (ASD) are neurodevelopmental disorders characterized by difficulties in social interaction and communication, as well as restrictive and repetitive behaviors and interests (WHO 2022). The prevalence of ASD has been increasing, with current estimates approximately 1–2% of children globally (Zeidan et al. 2022). While the precise causes and diagnostic markers of ASD remain unclear, research indicates a combination of genetic and environmental factors contributes to its development.

Alterations in the regulation of various hormones, including oxytocin, testosterone, and estradiol, have been implicated in the pathogenesis of ASD (Carter 2007; Jansakova et al. 2020; Lakatosova et al. 2022; Havranek et al. 2024). However, probably more complex neuroendocrine alterations, along with changes in neurotransmitter systems, significantly

Corresponding author: Mgr. Maria Kopcikova, Faculty of Medicine, Institute of Physiology, Comenius University, Bratislava, Slovakia; phone: 0903769708; e-mail: Kopcikova7@uniba.sk.

contribute to the etiology of ASD, particularly during early developmental stages. Thyroid hormones belong to the factors that play a significant role in various physiological processes. Upon release from the thyroid gland, tetraiodothyronine (T4) and triiodothyronine (T3) primarily bind to plasma proteins. The protein-bound hormones are referred to as bound T4 and T3, while the unbound fractions of the hormones are known as free T4 (fT4) and free T3 (fT3), with the latter being the more biologically active form. Thyroid hormones play a fundamental role in brain development both prenatally and postnatally, including neurogenesis, gliogenesis, synaptogenesis, and myelination (Bernal 2005; Moog et al. 2017).

Abnormal concentrations of thyroid hormones during the prenatal period may potentially be associated with an increased risk of ASD development (Berbel et al. 2014; Levie et al. 2018). However, few studies have investigated the association between postnatal thyroid hormone levels and ASD. Hoshiko et al. (2011) have found that very low blood T4 concentrations within a few hours of birth were linked to a higher risk of ASD development. An association between low T4 in newborns and risk of ASD has also been demonstrated by Lyall et al. (2017). In contrast, Soldin et al. (2003) have reported no significant differences in neonatal T4 concentrations between infants later diagnosed with ASD, ADHD, learning disabilities, and those without any diagnosis.

In terms of regulatory factors for thyroid hormones, Singh et al. (2017) have found significantly lower serum thyroid-stimulating hormone (TSH) concentrations in boys aged 2–8 years with ASD. This study has also reported that decreased TSH levels were significantly associated with higher rates of impaired social interaction and increased stereotyped behavior, as measured by the Autism Diagnostic Observation Schedule (ADOS). Similarly, Blazewicz et al. (2016) have observed significantly lower serum fT3 and fT4 levels alongside the higher TSH levels, in autistic boys aged 2–17 years compared to controls, although thyroid hormones were within the normal reference ranges in both groups. However, studies examining the correlation between the severity of autistic symptoms and thyroid hormone levels are quite scarce. Moreover, there is a lack of research exploring how thyroid hormone levels specifically relate to different domains of social interaction, communication, and restricted repetitive behavior.

This study was aimed 1) to determine the serum levels of TSH, fT3, and fT4 in children with ASD and 2) to investigate their association with the severity of ASD symptoms.

Subjects and Methods

Subjects. The total research sample consisted of 56 children (46 boys and 10 girls) with ASD diagnosis ranging in age from 2.13 to 3.56 years (Mean=2.92 years). All of the children were nonverbal or used only a few isolated words. Only 4 children (7.11%) had mild symptoms (Calibrated Severity Score 4 or 5). The rest of the group (52 children) had moderate to severe symptoms (Calibrated Severity Score 6–10).

ASD diagnosis. The ADOS-2 (Autism Diagnostic Observation Schedule - second version) (Lord et al. 2000; Gotham et al. 2009) is a "semistructured interview", it is a standardized instrument for assessing communication, social interaction, play, and creative use of materials in individuals who are suspected of having ASD or another developmental disorder. Administration of the ADOS-2 involves the administrator-child's interactions providing the child with stimuli and creating precise situations for observation of the child's spontaneous responses. The administrator evaluates these on the basis of their quality and frequency of occurrence during the administration. The output incorporates 3 scores: social affect (SA), restricted and repetitive behavior (RRB), and total score Calibrated Severity Scores (CSS). Scores for each scale range from 0 to 10, with 0 representing absence of symptoms and 10 representing the highest level of symptom severity.

The Autism Diagnostic Interview-Revised (ADI-R) (Lord et al. 1994) is a structured interview with the child's parents or guardians. Depending on the child's level of speech competency, it contains 80–90 questions that are grouped into three categories. Qualitative abnormalities in reciprocal social interaction (ADI-R_A), in communication (ADI-R_B) and narrowly defined, repetitive and stereotyped patterns of behavior and activities (ADI-R_C) are evaluated. The sum of the responses on each scale reveals whether the child being assessed has reached the cut-off score and whether it is reasonable to consider ASD. In the case of ADI-R_C, there is one additional question for 3-year-old children. To correct for this difference, we converted the total score into percentages - the raw score divided by the number of items. To make the scale the same for both ADI-R_A and ADI-R_B, we recalculated those as well. The score for each scale thus expands from 0 to 1, with 1 being the maximum score (maximum symptoms severity).

Data were collected during 04/2022 to 01/2023 at the Academic Research Centre for Autism, at the Faculty of Medicine, Comenius University in Bratislava.

Hormone analysis. The measurement of serum free triiodothyronine (s-fT3), free thyroxine (s-fT4), and thyroid-stimulating hormone (s-TSH) is widely considered the most thorough set of diagnostic tests for evaluating thyroid function. The venous blood samples were collected in serum gel tubes (BD Vacutainer® SST™ II Advance 8.5 ml serum tubes) immediately after the diagnostic procedures, between 10:00–10:30 a.m., and thereafter, sent to the laboratory. After separation of blood serum by centrifugation 10 min at RCF = 2000, i.e. 2000 x g at laboratory temperature (20–25°C), s-TSH, s-fT3, s-fT4 were determined on the day of collection by electrochemiluminescence immunoassay (ECLIA), by a Roche Cobas® 8000 (Elecsys TSH, Elecsys FT3 III, Elecsys FT4 IV) (Roche Diagnostics GmbH, Mannheim, Germany) closed analytical system (e801 module). The concentrations of each parameter were calculated from the calibration curve generated by the 2-point calibration and using the baseline calibration curve. This analysis was provided by the commercial laboratory Medirex in Slovakia.

Statistical methods. Multivariable linear regression analysis was conducted to assess the contributions of thyroid hormones on ASD symptoms severity by ADOS-2 and ADI-R. In addition to hormones, we considered age and sex as the possible independent variables. The final model was selected by the backward elimination method. Probability values (p) less than 0.05 were considered to be statistically significant. All statistical analyses together with the associated assumptions checking was performed using IBM SPSS Statistics for Windows, Version: 29.0 Armonk, NY: IBM Corp.

Ethics. The study was realized as a part of a larger research project (psychological and biological correlates of adaptive behavior in children with autism spectrum disorders in a multidisciplinary perspective), approved by the Ethical Committee of the Comenius University Faculty of Medicine and the University Hospital in Bratislava. All participants provided written informed consent before study participation.

Results

Serum concentrations of all monitored hormones were within the normal reference ranges in almost all children (Table 1). Decline of s-TSH was significantly associated with increased severity of impaired social interaction and impaired communication as rated by parents (ADI-R) and with a higher prevalence of stereotyped behaviors as observed in the diagnostic examination (ADOS-2). A decrease in s-fT3 was associated with the higher rates of stereotyped behavior as assessed by parents (ADI-R). Neither gender nor age were significant predictors. The coefficients of the final models are summarized in Table 2. The initial multiple linear regression models for each dependent variable, subject to backward elimination, are presented in Tables 3–7.

Discussion

To the best of our knowledge, this is the first study analyzing the relationship between the thyroid hormones and the non-verbal ASD children who used only a few isolated words. It was found that s-TSH, s-fT3, and s-fT4 levels in children with ASD were within the reference ranges. A significant association was revealed between a decline in s-TSH and the increased severity of impairments in social interaction and communication, as assessed by parents through the ADI-R questionnaire. Additionally, a decline in s-TSH was associated with a higher frequency of stereotyped behavior observed during diagnostic examinations using the ADOS-2. A decline in s-fT3 was associated with higher rates of stereotyped behavior as assessed by parents.

Thyroid hormones levels remain relatively high during early childhood to support rapid growth and brain development. T4 and T3 levels gradually decrease over time, although some studies have observed elevations during puberty and early adulthood (Morreale de Escobar et al. 2004; Lem et al. 2012; Walsh 2022). In the present study, s-fT3 and s-fT4 were found to be within the physiological ranges. These findings correspond with the results of the Blazewicz et al. (2016), who have also reported that these thyroid hormones were within the normal reference range in autistic boys with respect to age.

Table 1
Descriptive statistic of thyroid hormone concentrations (N=56). In addition, reference values are also provided for comparison (1–6 years age) (Roche Diagnostics GmbH 2009).

Thyroid hormone	Sample values Median (2.5–97.5 percentile)	Reference values Median (2.5–97.5 percentile)
s-TSH (mIU/l)	2.60 (1.05–6.04)	2.58 (0.70–5.97)
s-fT3 (pmol/l)	6.35 (4.03–7.96)	6.27 (3.69–8.46)
s-fT4 (pmol/l)	16.60 (11.96–22.06)	16.90 (12.30–22.80)

Abbreviations: s-fT3 – serum free triiodothyronine; s-fT4 – serum free thyroxine; s-TSH – serum thyroid-stimulating hormone.

Table 2
Thyroid hormones as predictors of ASD symptom severity. A summary of the final multiple linear regression models, obtained through backward elimination.

Dependent variable	Predictor	B	S.E.	β	p-value	95% CI Lower	95% CI Upper	Adjusted R^2
ADI-R (A)	(Constant)	0.698	0.061		0.000	0.575	0.821	0.130
	s-TSH	–0.058	0.019	–0.382	0.004	–0.096	–0.020	
ADI-R (B)	(Constant)	0.804	0.064		0.000	0.675	0.933	0.096
	s-TSH	–0.052	0.020	–0.335	0.012	–0.092	–0.012	
ADI-R (C)	(Constant)	0.690	0.179		0.000	0.330	1.049	0.085
	s-TSH	0.031	0.018	0.234	0.082	–0.004	0.067	
	s-fT3	–0.067	0.029	–0.307	0.024	–0.124	–0.009	
ADOS-2 (RRB)	(Constant)	5.623	1.551		0.001	2.512	8.734	0.119
	Age	0.963	0.497	0.245	0.058	–0.035	1.960	
	s-TSH	–0.360	0.155	–0.294	0.024	–0.672	–0.049	

Abbreviations: ADI-R – autism diagnostic interview-revised; ADI-R (A) – degree of impairment of social interaction; ADI-R (B) – degree of communication impairment; ADI-R (C) – restricted and repetitive behavior severity score; ADOS-2 – autism diagnostic observation schedule-second version; ADOS-2 (RRB) – restricted and repetitive behavior severity score; ASD – autism spectrum disorders; B – unstandardized beta; β – standardized beta; p – statistical significance; S.E. – standard error; s-fT3 – serum free triiodothyronine; s-TSH – serum thyroid-stimulating hormone.

Table 3
Thyroid hormones, age and sex as predictors of social interaction impairment evaluated by parent interview (ADI-R)

Predictor	B	S.E.	β	p-value	t	95% CI Lower	95% CI Upper	Adjusted R^2
(Constant)	0.805	0.303		0.011	2.654	0.196	1.415	0.070
s-TSH	–0.055	0.020	–0.362	0.010	–2.675	–0.096	–0.014	
s-fT3	–0.023	0.035	–0.092	0.518	–0.650	–0.092	0.047	
s-fT4	0.003	0.014	0.031	0.823	0.225	–0.024	0.031	
Age	–0.007	0.065	–0.015	0.911	–0.112	–0.137	0.123	
Sex	–0.004	0.061	–0.010	0.942	–0.073	–0.127	0.118	

Abbreviations: ADI-R – autism diagnostic interview-revised; B – unstandardized beta; β – standardized beta; p – statistical significance; S.E. – standard error; s-fT3 – serum free triiodothyronine; s-fT4 – serum free thyroxine; s-TSH – serum thyroid-stimulating hormone.

Table 4
Thyroid hormones, age and sex as predictors of communication impairment evaluated by parent interview (ADI-R)

Predictor	B	S.E.	β	p-value	t	95% CI Lower	95% CI Upper	Adjusted R^2
(Constant)	1.071	0.314		0.001	3.415	0.441	1.702	0.059
s-TSH	–0.050	0.021	–0.322	0.022	–2.368	–0.093	–0.008	
s-fT3	–0.014	0.036	–0.055	0.700	–0.387	–0.086	0.058	
s-fT4	0.002	0.014	0.020	0.883	0.148	–0.026	0.030	
Age	–0.082	0.067	–0.165	0.225	–1.230	–0.217	0.052	
Sex	0.027	0.063	0.057	0.672	0.426	–0.100	0.154	

Abbreviations: ADI-R – autism diagnostic interview-revised; B – unstandardized beta; β – standardized beta; p – statistical significance; S.E. – standard error; s-fT3 – serum free triiodothyronine; s-fT4 – serum free thyroxine; s-TSH – serum thyroid-stimulating hormone.

Table 5
Thyroid hormones, age and sex as predictors of restricted and repetitive behaviors evaluated by parent interview (ADI-R)

Predictor	B	S.E.	β	p-value	t	95% CI Lower	95% CI Upper	Adjusted R^2
(Constant)	0.681	0.274		0.016	2.487	0.131	1.231	0.040
s-TSH	0.032	0.018	0.240	0.087	1.746	–0.005	0.069	
s-fT3	–0.065	0.031	–0.299	0.042	–2.085	–0.128	–0.002	
s-fT4	–0.002	0.012	–0.020	0.885	–0.146	–0.027	0.023	
Age	–0.001	0.058	–0.003	0.985	–0.019	–0.118	0.116	
Sex	0.039	0.055	0.094	0.487	0.701	–0.072	0.150	

Abbreviations: ADI-R – autism diagnostic interview-revised; B – unstandardized beta; β – standardized beta; p – statistical significance; S.E. – standard error; s-fT3 – serum free triiodothyronine; s-fT4 – serum free thyroxine; s-TSH – serum thyroid-stimulating hormone.

Table 6
Thyroid hormones, age and sex as predictors of social affect evaluated by direct observation (ADOS-2)

Predictor	B	S.E.	β	p-value	t	95% CI Lower	95% CI Upper	Adjusted R^2
(Constant)	11.341	2.551		<0.001	4.445	6.216	16.465	0.005
s-TSH	0.119	0.172	0.097	0.491	0.693	–0.226	0.465	
s-fT3	–0.344	0.291	–0.172	0.243	–1.181	–0.928	0.241	
s-fT4	0.009	0.115	0.011	0.939	0.077	–0.222	0.240	
Age	–0.752	0.544	–0.191	0.173	–1.382	–1.846	0.341	
Sex	–0.390	0.515	–0.104	0.452	–0.758	–1.424	0.643	

Abbreviations: ADOS-2 – autism diagnostic observation schedule-second version; B – unstandardized beta; β – standardized beta; p – statistical significance; S.E. – standard error; s-fT3 – serum free triiodothyronine; s-fT4 – serum free thyroxine; s-TSH – serum thyroid-stimulating hormone.

Table 7
Thyroid hormones, age and sex as predictors of restricted and repetitive behaviors evaluated by direct observation (ADOS-2)

Predictor	B	S.E.	β	p-value	t	95% CI Lower	95% CI Upper	Adjusted R^2
(Constant)	3.546	2.422		0.150	1.464	3.546	2.422	0.096
s-TSH	–0.383	0.163	–0.312	0.023	–2.342	0.906	0.517	
s-fT3	0.183	0.260	0.092	0.511	0.662	–0.383	0.163	
s-fT4	0.080	0.109	0.100	0.466	0.735	0.183	0.276	
Age	0.906	0.517	0.231	0.086	1.753	0.080	0.109	
Sex	–0.219	0.489	–0.058	0.656	–0.448	–0.219	0.489	

Abbreviations: ADOS-2 – autism diagnostic observation schedule-second version; B – unstandardized beta; β – standardized beta; p – statistical significance; S.E. – standard error; s-fT3 – serum free triiodothyronine; s-fT4 – serum free thyroxine; s-TSH – serum thyroid-stimulating hormone.

Although it should be noted that Blazewicz et al. (2016) have found significantly lower free T3 and T4 levels in the autistic group compared to controls. It is generally accepted that T4 levels, particularly in mothers during pregnancy, play important roles and recent meta-analyses confirm that lower maternal T4 levels can be related to the later onset of autistic traits in offspring (Levie et al. 2018).

A notable finding of this study is that despite normal s-TSH values, lower s-TSH levels were associated with increased severity of social interaction and communication impairments, as well as increased stereotyped behavior, in ASD children. The observation of normal s-TSH levels aligns with the findings of Blazewicz et al. (2016) and Desoky et al. (2017). However, in contrast to our results, Desoky et al. (2017) have found

no significant association between serum TSH and symptoms severity. Our findings partially align with those of Singh et al. (2017), who have reported that decreased TSH levels were significantly associated with higher rates of impaired social interaction and stereotyped behavior in ASD children. Although further confirmation of our findings in larger patient cohorts is needed, measuring TSH levels in children with ASD at various developmental stages could provide valuable insights for future research. In this context, it is interesting to note that in a study where TSH was measured in pregnant mothers, higher TSH levels were associated with lower social responsiveness scores in their offspring aged 3–8 years (Zhong et al. 2024). In contrast, a different study, where TSH levels were examined, found no link to psychomotor development impairments in offspring at preschool age (Trumpff et al. 2016).

In conclusion, thyroid hormones changes may be linked to specific social-communication alterations only during specific developmental stages. Previous research has often included a wider age range, which however, made more difficult to see the link between the hormone levels and the severity of autism. To the best of our knowledge, this is the first study analyzing the relationship between the thyroid hormones and the non-verbal ASD children in a more narrow young age. Moreover, different ways of autism diagnosis in the past studies made difficult to compare their findings with our ones. Larger cohort studies are needed for definitive conclusions, but current evidence suggests that lower thyroid hormones levels and hypothalamic-pituitary-thyroid axis dysregulation may be involved in autism pathogenesis.

Acknowledgements

This work was supported by the Slovak Research and Development Agency projects APVV-20-0070 and APVV-20-0139.

Conflict of interest: *The authors declare no conflicts of interest.*

References

Berbel P, Navarro D, Roman GC. An evo-devo approach to thyroid hormones in cerebral and cerebellar cortical development: etiological implications for autism. Front Endocrinol 5, 146, 2014.

Bernal J. Thyroid hormones and brain development. Vitam Horm 71, 95–122, 2005.

Blazewicz A, Makarewicz A, Korona-Glowniak I, Dolliver W, Kocjan R. Iodine in autism spectrum disorders. J Trace Elem Med Biol 34, 32–37, 2016.

Carter CS. Sex differences in oxytocin and vasopressin: Implications for autism spectrum disorders? Behav Brain Res 176, 170–186, 2007.

Desoky T, Hassan MH, Fayed HM, Sakhr HM. Biochemical assessments of thyroid profile, serum 25-hydroxycholecalciferol and cluster of differentiation 5 expression levels among children with autism. Neuropsychiatr Dis Treat 13, 2397–2403, 2017.

Gotham K, Pickles A, Lord C. Standardizing ADOS scores for a measure of severity in autism spectrum disorders. J Autism Dev Disord 39, 693–705, 2009.

Havranek T, Bacova Z, Bakos J. Oxytocin, GABA, and dopamine interplay in autism. Endocr Regul 58, 105–114, 2024.

Hoshiko S, Grether JK, Windham GC, Smith D, Fessel K. Are thyroid hormone concentrations at birth associated with subsequent autism diagnosis? Autism Res 4, 456–463, 2011.

Jansakova K, Hill M, Celarova D, Celusakova H, Repiska G, Bicikova M, Macova L, Ostatnikova D. Alteration of the steroidogenesis in boys with autism spectrum disorders. Transl Psychiatry 10, 340, 2020.

Lakatosova S, Jansakova K, Babkova J, Repiska G, Belica I, Vidosovicova M, Ostatnikova D. The relationship of steroid hormones, genes related to testosterone metabolism and behavior in boys with autism in Slovakia. Psychiatry Investig 19, 73–84, 2022.

Lem AJ, de Rijke YB, van Toor H, de Ridder MAJ, Visser TJ, Hokken-Koelega ACS. Serum thyroid hormone levels in healthy children from birth to adulthood and in short children born small for gestational age. J Clin Endocrinol Metab 97, 3170–3178, 2012.

Levie D, Korevaar T, Bath S, Dalmau-Bueno A, Murcia M, Espada M, Dineva M, Ibarluzea J, Sunyer J, Tiemeier H, Rebagliato M, Rayman M, Peeters R, Guxens M. Thyroid function in early pregnancy, child IQ, and autistic traits: a meta-analysis of individual participant data. J Clin Endocrinol Metab 103, 2967–2979, 2018.

Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. J Autism Dev Disord 24, 659–685, 1994.

Lord C, Risi S, Lambrecht L, Cook EH, Leventhal BL, DiLavore PC, Pickles A, Rutter M. The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. J Autism Dev Disord 30, 205–223, 2000.

Lyall K, Croen L, Daniels J, Fallin MD, Ladd-Acosta C, Lee BK, Park BY, Snyder NW, Schendel D, Volk H, Windham GC, Newschaffer C. The changing epidemiology of autism spectrum disorders. Annu Rev Public Health 38, 81–102, 2017.

Moog NK, Entringer S, Heim C, Wadhwa PD, Kathmann N, Buss C. Influence of maternal thyroid hormones during gestation on fetal brain development. Neuroscience 342, 68–100, 2017.

Morreale de Escobar G, Obregon MJ, Escobar del Rey F. Role of thyroid hormone during early brain development. Eur J Endocrinol 151, U25–U37, 2004.

Roche Diagnostics GmbH. Reference intervals for children and adults, Elecsys Thyroid Tests. Roche, 2009. https://hormonerestoration.com/files/Thyroid%20Reference%20data%20Roche.pdf.

Singh S, Yazdani U, Gadad B, Zaman S, Hynan LS, Roatch N, Schutte C, Marti CN, Hewitson L, German DC. Serum thyroid-stimulating hormone and interleukin-8 levels in boys with autism spectrum disorder. J Neuroinflammation 14, 113, 2017.

Soldin OP, Lai S, Lamm SH, Mosee S. Lack of a relation between human neonatal thyroxine and pediatric neurobehavioral disorders. Thyroid 13, 193–198, 2003.

Trumpff C, De Schepper J, Vanderfaeillie J, Vercruysse N, Van Oyen H, Moreno-Reyes R, Tafforeau J, Vandevijvere S. Neonatal thyroid-stimulating hormone concentration and psychomotor development at preschool age. Arch Dis Child 101, 1100–1106, 2016.

Walsh JP. Thyroid function across the lifespan: Do age-related changes matter? Endocrinol Metab (Seoul) 37, 208–219, 2022.

World Health Organization. ICD-11: International classification of diseases (11th revision). Rev Saude Publica 54, 104, 2022.

Zeidan J, Fombonne E, Scorah J, Ibrahim A, Durkin MS, Saxena S, Yusuf A, Shih A, Elsabbagh M. Global prevalence of autism: A systematic review update. Autism Res 15, 778–790, 2022.

Zhong C, Rando J, Patti MA, Braun JM, Chen A, Xu Y, Lanphear BP, Yolton K, Croen LA, Fallin MD, Hertz-Picciotto I, Newschaffer CJ, Lyall K. Gestational thyroid hormones and autism-related traits in the EARLI and HOME studies. Autism Res INSAR 17, 716–727, 2024.