

# *Optic Nerve Hypoplasia*



**ChildrensHospitalLosAngeles**  
International Leader in Pediatrics

KECK  
SCHOOL OF MEDICINE USC

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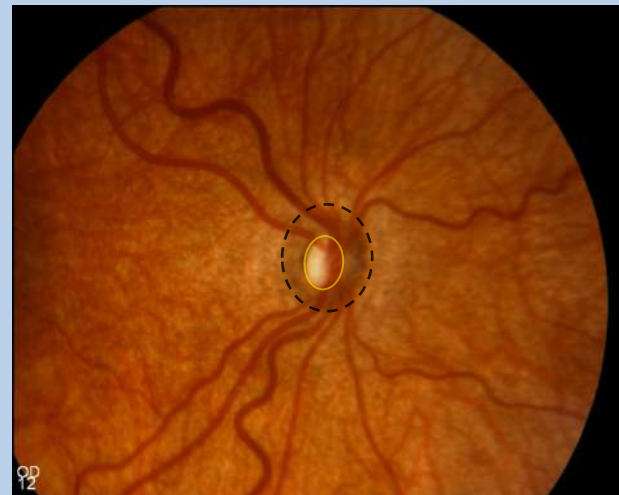
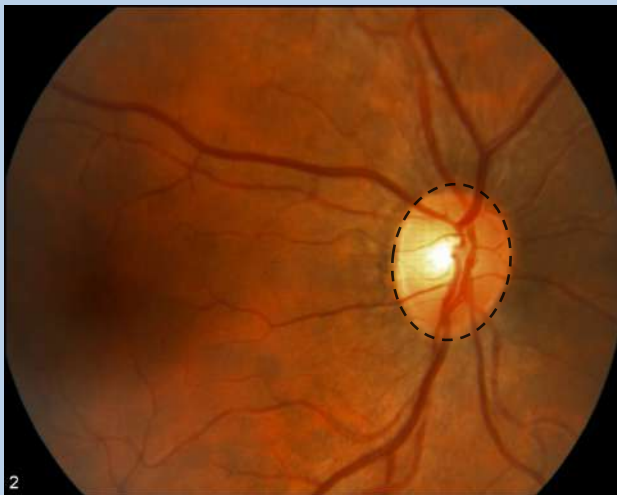
- How is ONH diagnosed?
- What is the Syndrome of ONH?
- What causes ONH?
- What are the medical and developmental consequences of ONH?
- Recent and future epidemiology research.

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One Small Voice Foundation

# Optic Nerve Hypoplasia

Definition: Underdeveloped optic nerve in one or both eyes



Birth defect estimated to occur between 7<sup>th</sup> & 15<sup>th</sup> gestational week

# *Pathogenesis of ONH*

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- 1<sup>st</sup> trimester: Optic nerve development begins
- Interruption in normal development results in an underdeveloped or hypoplastic optic nerve
  - ✓ Nerve fibers fail to reach target destination  
*and /or*
  - ✓ Fibers undergo excessive programmed death

# *History of ONH in Literature*

Magnus K: *Clin Monatsbl Augenh* 1884, 32:85

Schwarz O: Ein Fall von mangelhafter Bildung beider Sehnerven. *Albrecht von Graefes Arch Klin Ophthalmol* 1915, 90:326

Reeves D: Congenital absence of the septum pellucidum. *Bull Johns Hopkins* 1941, 69:61–71.

## CONGENITAL ABSENCE OF THE SEPTUM PELLUCIDUM

### A CASE DIAGNOSED ENCEPHALOGRAPHICALLY AND ASSOCIATED WITH CONGENITAL AMAUROSIS

DAVID L. REEVES, M.D.

*From the Children's Hospital of Los Angeles, and the Department of Surgery  
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Submitted for publication April 23, 1941

According to Dolgopol (1), only four cases of absence of the septum pellucidum in fully developed brains, and two in fetal brains have been reported. The first of these was that of Trenchini (2) in 1880, and the second that of Hochstetter (3) in 1925. Prior to this, Hochstetter had observed absence of the septum pellucidum in otherwise well-formed brains of fetuses about the third and fifth month of gestation. He believed congenital absence of the septum pellucidum was not rare and usually escaped attention. In 1930 Hahn and Kuhlenbeck (4) also discovered the anomaly in the dissecting room, but no information on the history of the patient was obtained. Dolgopol added an additional case discovered at autopsy in 1938.

In 1935 Dyke and Davidoff (5) demonstrated this anomaly encephalographically for the first time in a 23 year old woman with post-encephalitic disorders of behavior. Undoubtedly Dandy's (6) description of the pneumographic picture of congenital cerebral cysts of the cavum septi pellucidi and cavum vergae in 1931, and those by Davidoff and Dyke (7) and Hyndman and Penfield (8) of absence of the corpus callosum led to a more easily appreciated picture of absence of the septum pellucidum. Sfintzescu and Mihailescu (9) reported a case found ventriculographically in 1936, and although others may have been overlooked, those diagnosed pneumoencephalographically have at all events been extremely uncommon, and for that reason as well as for the fact that the present case is the youngest so diagnosed, it was believed worthy of publication.

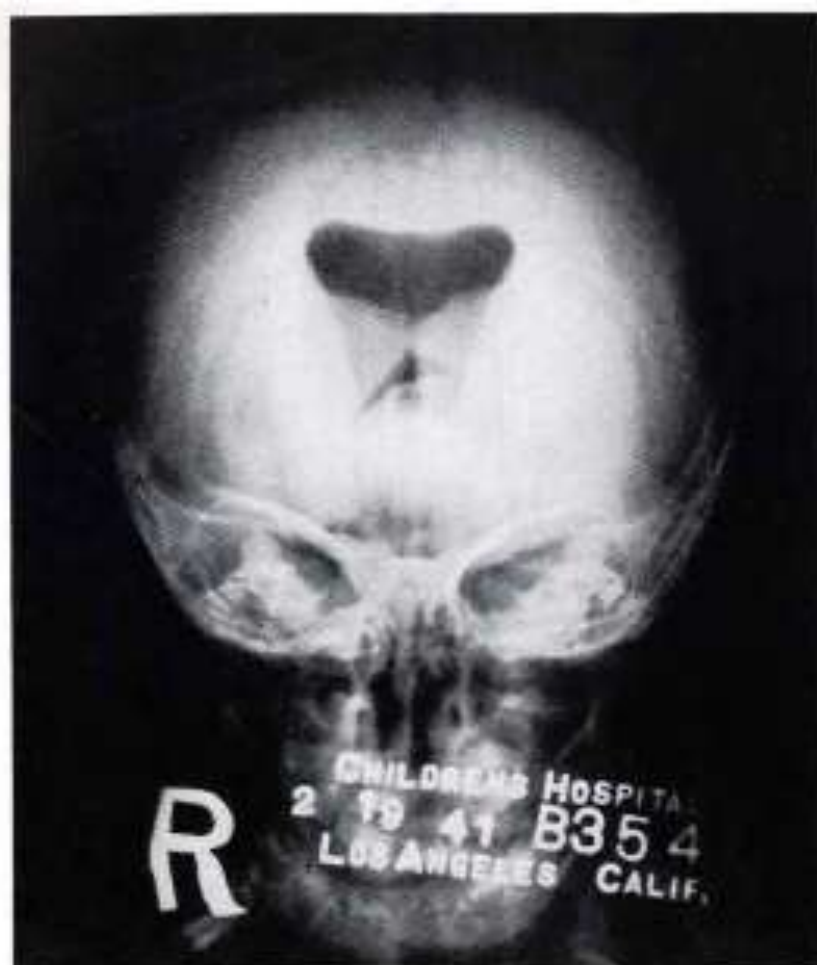


FIG. 2. ENCEPHALOGRAM. ANTEROPOSTERIOR VIEW SHOWING MEDIAL CONFLUENCE OF THE LATERAL VENTRICLES ANTERIORLY RESULTING FROM ABSENCE OF THE SEPTUM PELLUCIDUM

normal. In the neurological examination, the optic discs were seen only with difficulty and appeared to be pale. Subsequent examination by Dr. Rodman Irvine under ether anesthesia led him to the diagnosis of bilateral primary optic atrophy of undetermined origin, probably, however, on the basis of a congenital aplasia. The pupils failed to react to light and there was no blinking of the eyes when objects were brought suddenly toward them. There was a strabismus and



# *“Septo-optic dysplasia”*

DeMorsier (1956):

- 84 y/o woman without known vision problems died from complications of pyelonephritis
- Absent septum pellucidum, thin corpus callosum, vertically displaced left optic tract (normal size chiasm)

## 20. III. Agénésie du septum lucidum avec malformation du tractus optique. La dysplasie septo-optique

Par G. DE MORSIER (Genève)

L'agénésie du septum lucidum paraît être aussi rare que celles du c. calleux, des lobes olfactifs et du vermis que nous avons étudiées précédemment<sup>1)</sup>. Nous n'avons trouvé que 11 cas anatomo-cliniques publiés avant le nôtre et 23 cas diagnostiqués par l'encéphalographie gazeuse. Généralement l'examen anatomique du cerveau, fait uniquement à l'œil nu, est très sommaire. Aucun cas n'a été examiné sur coupes microscopiques.

Voici le résumé des cas comportant un examen anatomique du cerveau:

1. *Tenchini*, 1880. — Demetrio B., âgé de 2 ans  $\frac{1}{2}$ , mort le 8 novembre 1883 d'une méningite purulente. L'enfant était *très intelligent* et gentil, il ne présentait aucune malformation corporelle. Examen du cerveau à l'Institut d'Anatomie de Pavie. Poids: 923 g. Le cerveau est bien conformé extérieurement. Sur une coupe transversale on remarque l'absence complète du *septum lucidum*. Ventricule unique; l'épendyme passe d'un ventricule à l'autre sans interruption. La voûte à quatre piliers (fornix) est normalement développée dans chacune de ses parties mais n'adhère pas au c. calleux. La commissure grise manque. Pas d'autres anomalies.

2. *Gibson*, 1924. — Homme d'âge moyen, ayant passé ses dernières années dans un hospice pour aliénés incurables. Six ans avant sa mort, il a été blessé à la tête par la pointe d'un pic qui est entrée profondément dans la région pariétale du crâne et a pénétré jusqu'à la région frontale antérieure, près de la fissure sagittale. Pas d'examen clinique. Cerveau: le septum lucidum existe, il a deux fois sa longueur normale et il est percé d'un grand nombre d'orifices de toutes dimensions. La cavité du septum est oblitérée. *Le fornix est déplacé en avant et en bas*; il est peu développé. Le c. calleux est plus grand que normalement, sauf à un endroit où il est très aminci et mal formé. Les deux ventricules latéraux communiquent largement par les orifices. Ils sont un peu dilatés. Il semble y avoir corrélation entre cet élargissement et les autres malformations.

<sup>1)</sup> *Morsier, G. de*: Etudes sur les dysraphies crânio-encéphaliques: I. Agénésie des lobes olfactifs (télencéphaloschizia latéral) et des commissures calleuses et antérieures (télencéphaloschizia médian). La dysplasie olfacto-génitale. Arch. Suisses Neurol. Psychiat., 1955, 74, 309-361.

*Morsier, G. de*: Etudes sur les dysraphies crânio-encéphaliques: II. Agénésie du vermis cérébelleux. Dysraphie rhombocéphalique médiane (rhomboschizia). Mschr. Psychiat. Neurol. 1955, 129, 321-344.

# *History of ONH in Literature*

- Hoyt, et.al. (*Lancet*, 1970):  
Three cases of “septo-optic dysplasia” and  
pituitary dwarfism
- Ellenberger & Runyan (1970):  
One case of ONH, holoprosencephaly, and  
pituitary dwarfism

**Septo-Optic Dysplasia =**

**Optic Nerve Hypoplasia**

**+**

**Hypopituitarism or**

**Midline brain malformations**

# *What is the Syndrome of ONH?*

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Definition: Underdeveloped optic nerve

Clinical Associations:

- Brain Malformations
- Developmental Delay
- Hypopituitarism
- Vision Impairment

*Isolated ONH is uncommon*

# *CHLA Research Program*

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- Pathology
- Clinical Studies
  - Prospective observational
  - Intervention trials
- Epidemiologic investigations
  - Disease distribution in U.S.
  - Etiology

# *CHLA Prospective ONH Study*

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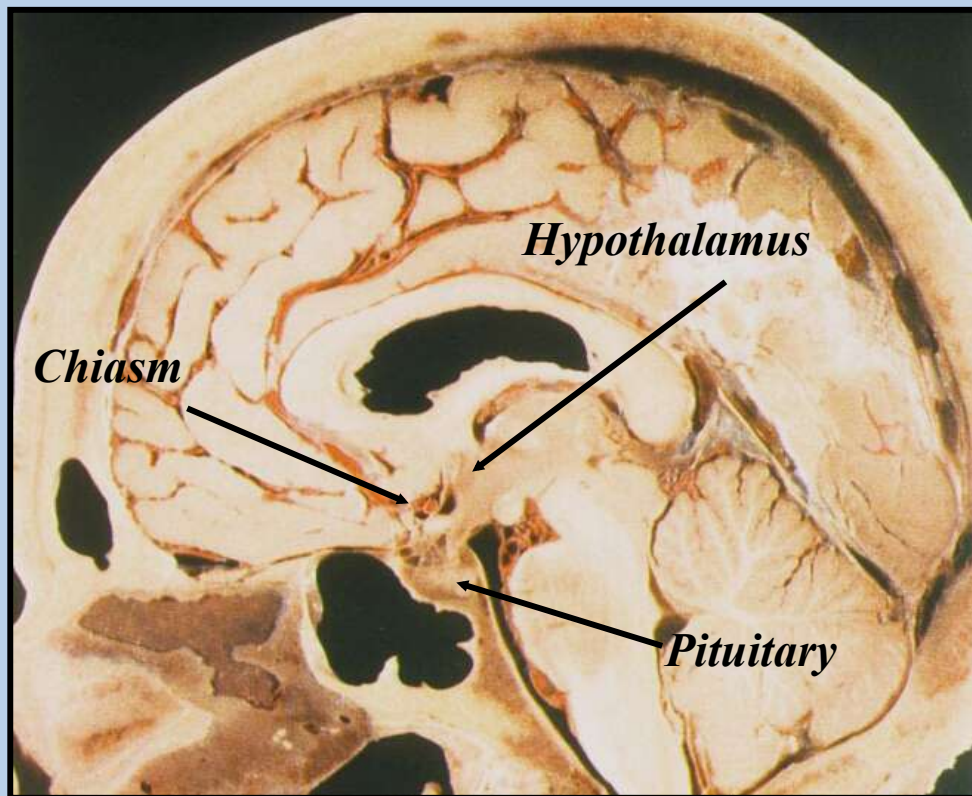
Children  $\leq$  2 yrs. followed until age 5 years

- ✓ Identify clinical risk factors for poor outcomes
  - Developmental
  - Endocrinologic
  - Vision
- ✓ Identify prenatal risk factors for ONH

# *Central Nervous System*

## *Mis-Wiring*

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# *CNS Abnormalities in ONH*

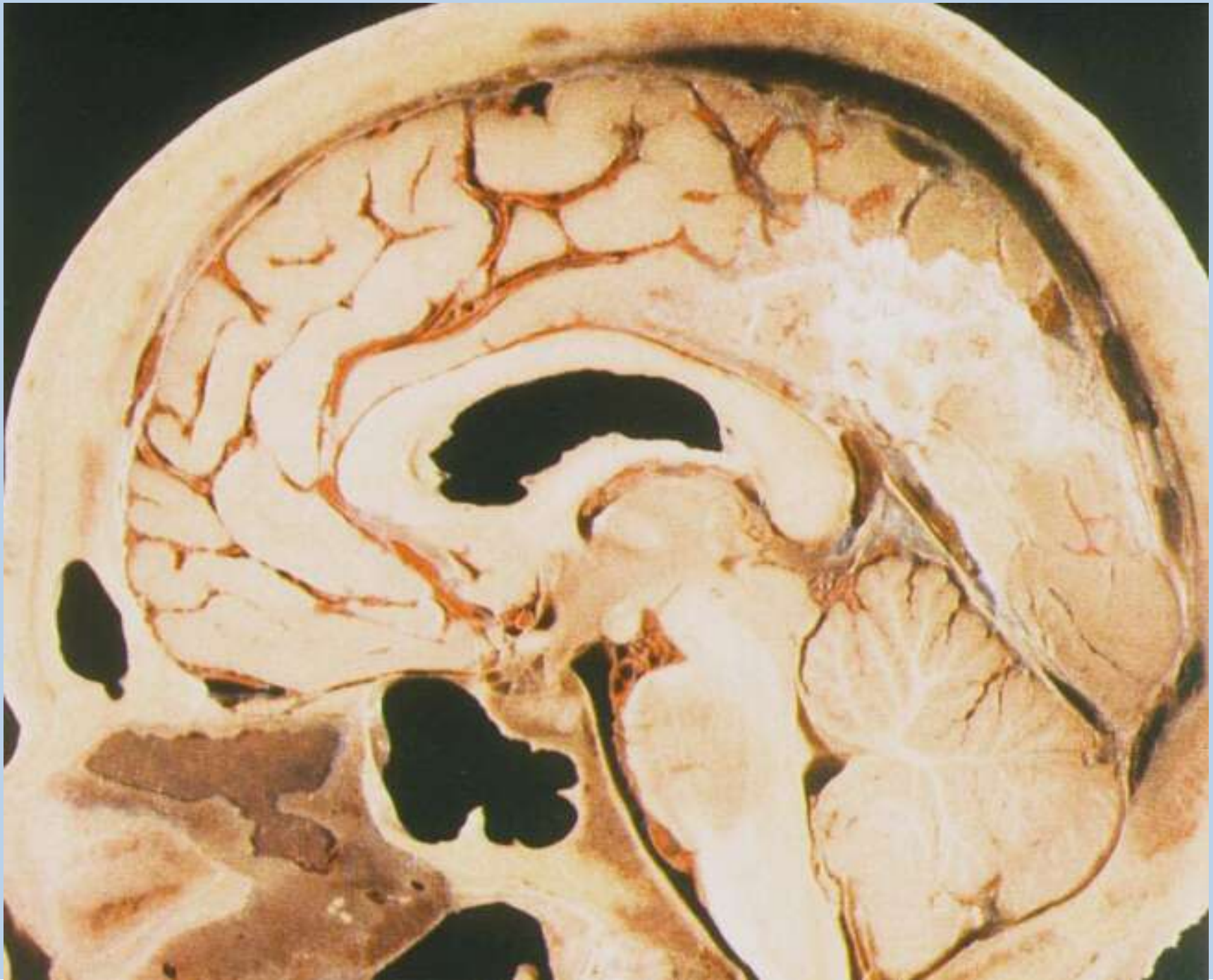
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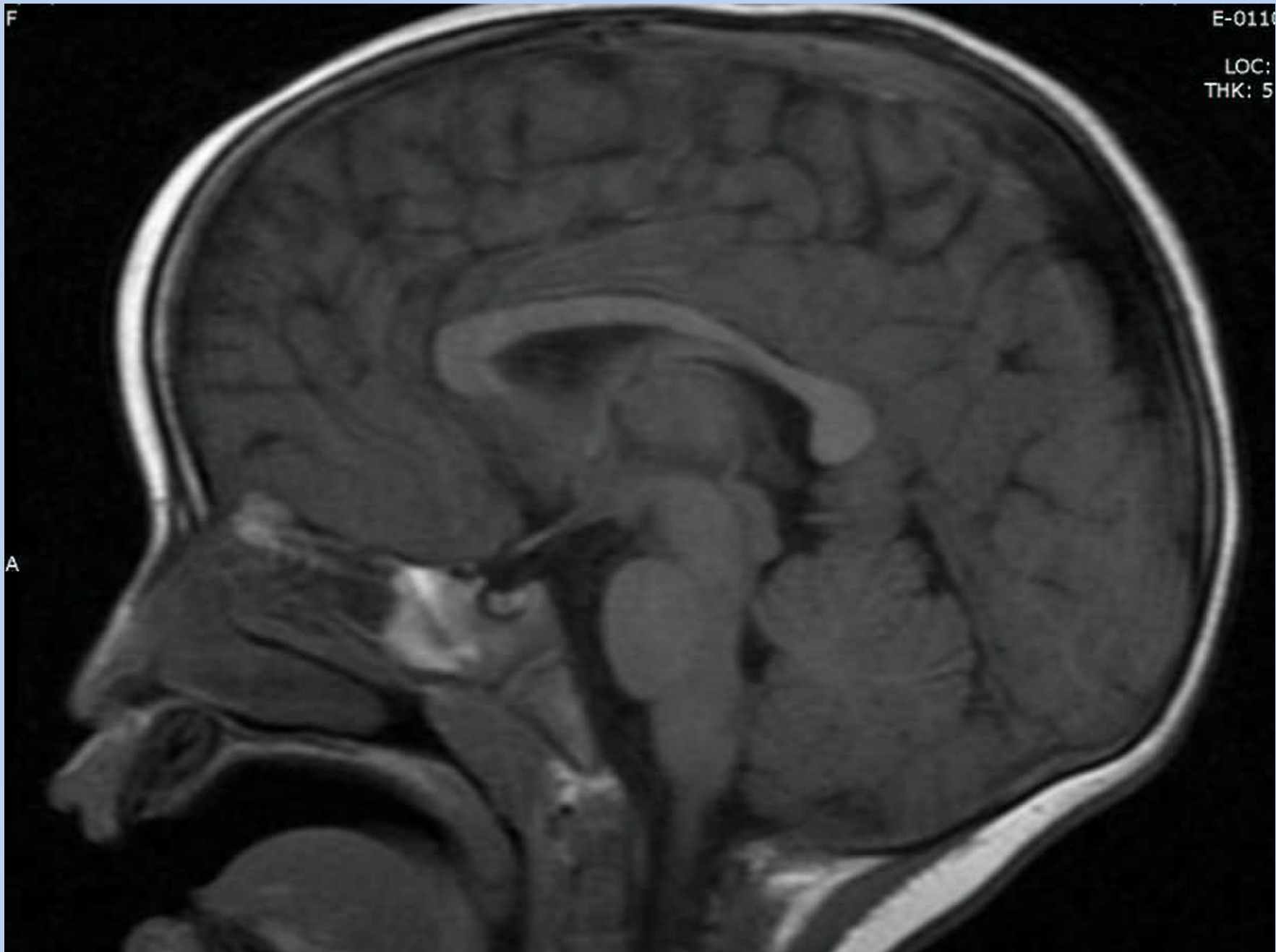
- Hypoplasia of corpus callosum 38%
- Absence of septum pellucidum 38%
- Pituitary dysgenesis 13%
- Other major malformations 14%
  - hydrocephalus
  - white matter hypoplasia
  - micropolygyria
  - schizencephaly

## *MRI Findings & Developmental Delay*

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- Septum Pellucidum
  - 72% delayed if absent (vs. 73%)
- ✓ Corpus Callosum
  - 96% delayed if hypoplastic (vs. 58%)
- Other major malformations
  - 100% delayed if present (vs. 68%)





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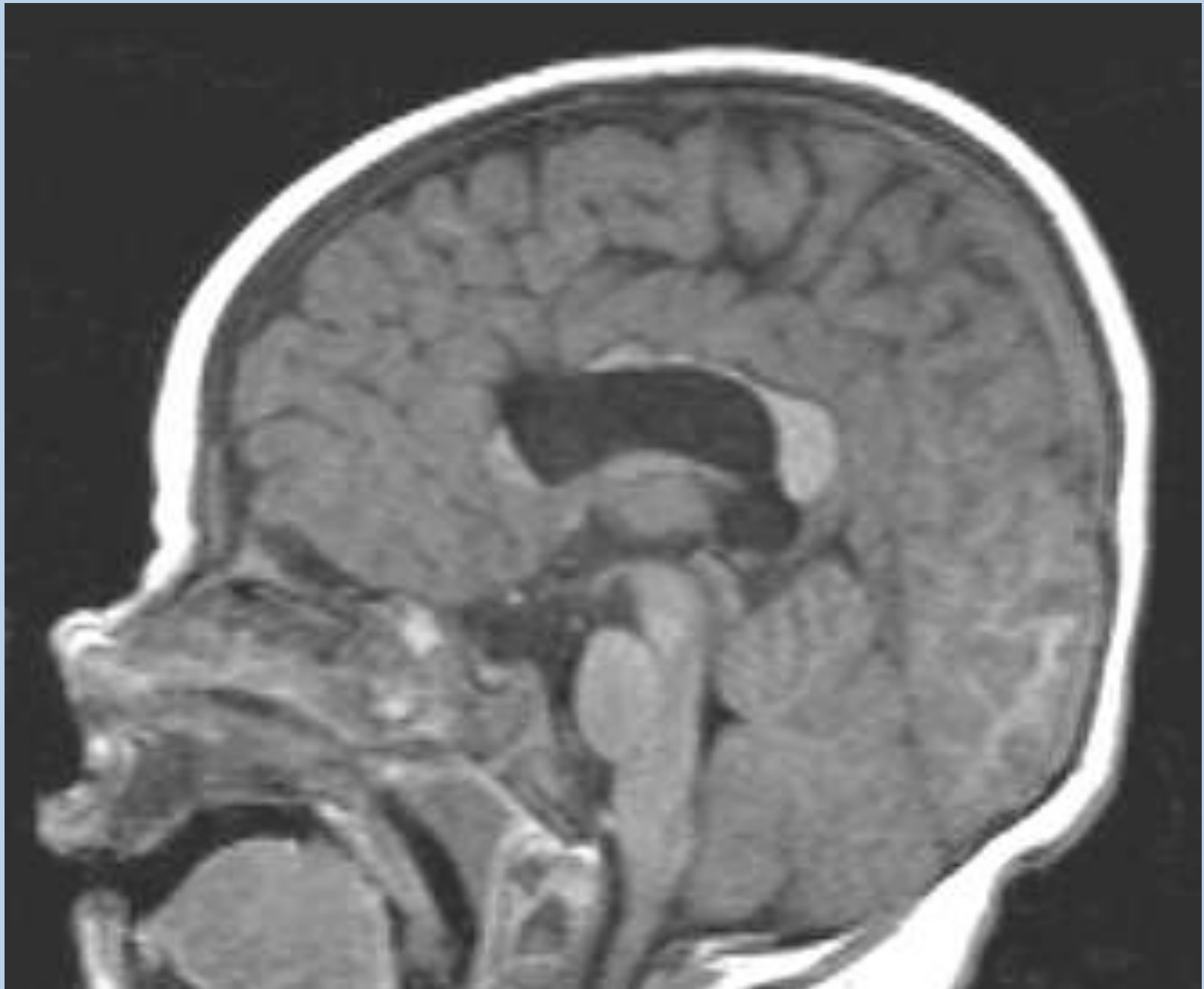
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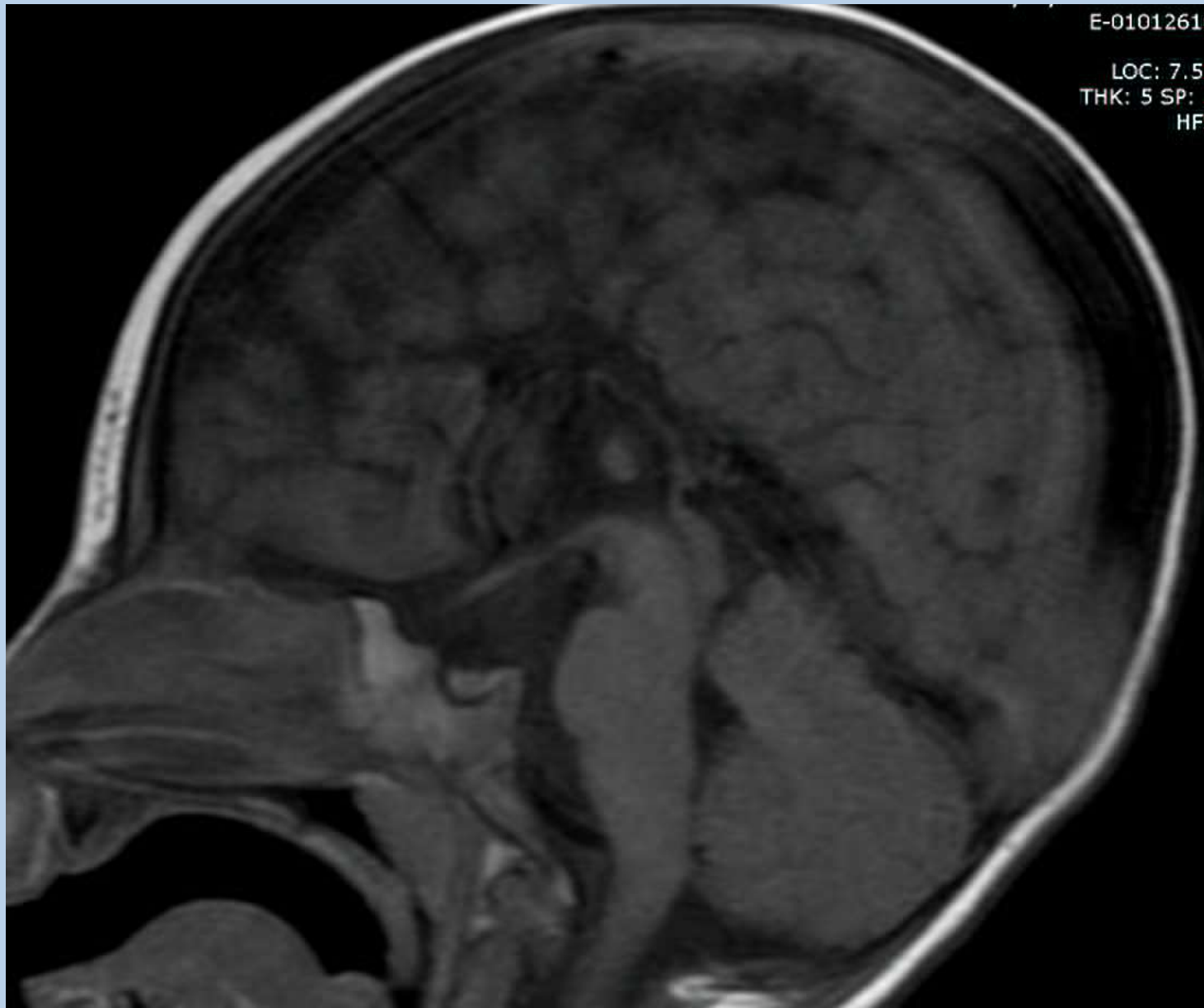
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# *Corpus Callosum and Developmental Disorders*

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- Corpus callosum area measurements much smaller in subjects with delay
- Corpus callosum size may also correlate with Autism Spectrum Disorders (ASD)
  - Possible decreased size in subjects with ASD versus delayed



# History of ONH & Autism

- Recent recognition
- Increasing prevalence
- Similar incidence trajectories
- Overlapping symptoms & signs

# Autism Behaviors Noted in ONH

- Rigid
- Dependence on Routines
- Lack of spontaneity in verbal interactions
- Perseverative behavior
- Tactile & auditory defensiveness

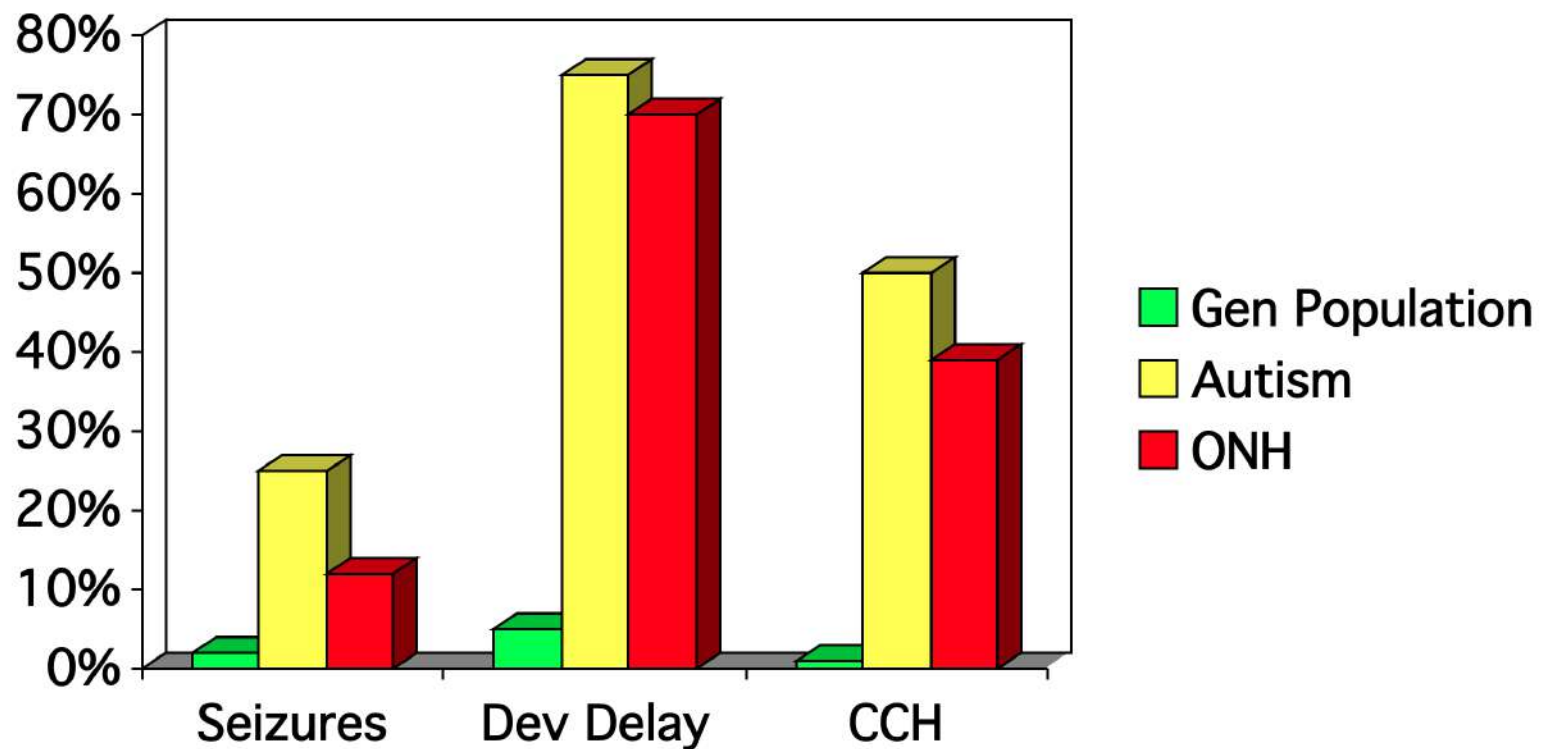
# Autism noted in ONH

- Margalith (1984) - 21% of children with ONH had dev impairment including autism
- Ek (2005) - 46% of ONH & blindness had diagnosis of autism
- Parr (2010) - 31% of ONH with clinical autism diagnosis
- CDC (2010) - 0.9% General population

# ONH & Autism Similarities

- Developmental delay
- Seizures
- Gastrointestinal dysfunction
- Sleep disturbance
- Corpus Callosum hypoplasia
- Accelerated head circumference growth
- Neonatal jaundice

# Clinical Characteristics



# Question: Is this behavior really autism?

- Inexperience by examiners with visually-impaired children
- Behavior attributable to VI, neurological impairment, social-emotional deprivation
- Problems with diagnostic tools

# Problem with Diagnostic Tools

- Highly visually-dependent joint attention behaviors (eye contact, referential eye gaze and pointing)
- Repetitive behaviors normal in blind children (rocking)
- Language abnormalities normal in blind children (pronoun reversal)
- Orienting behaviors normal in blind children (smelling, touching)

**DIRECTIONS**

For each question,  
circle the number that  
best describes the  
child's behavior over  
the past 6 months.

Child's Name: \_\_\_\_\_ Chronological Age: \_\_\_\_\_

Gender (required): ☐ Female ☐ Male

Ethnicity: \_\_\_\_\_

Respondent's Name: \_\_\_\_\_ Administration Date: \_\_\_\_\_

Relationship to Child: ☐ Mother ☐ Father ☐ Other \_\_\_\_\_

**2. Expressions on his or her face don't match what he or she is saying.**

**9. Clings to adults, seems too dependent on them.**

**15. Is able to understand the meaning of other people's tone of voice and facial expressions.**

**16. Avoids eye contact or has unusual eye contact.**

**21. Is able to imitate others' actions.**

**45. Focuses his or her attention to where others are looking or listening.**

**55. Knows when he or she is too close to someone or is invading someone's space.**

**65. Stares or gazes off into space.**



## **Social Communication Questionnaire (SCQ)**

9. Has her/his facial expression usually seemed appropriate to the particular situation?

10. Has she/he ever used your hand like a tool or as if it were part of her/his own body (e.g. pointing with your finger)?

22. When she/he was 4 to 5 did she/he ever spontaneously point at things around her/him just to show you things?

26. When she/he was 4 to 5 did she/he usually look at you directly in the face when doing things with you or talking with you?

27. When she/he was 4 to 5, did she/he smile back if someone smiled at her/him?

# Autism Diagnostic Observation Schedule

- ADOS is dependent on level of functioning- different modules depending on level of language.
- For less verbal children, activities rely on free and structured play.
- Informal modifications have been used- enlarging pictures, using larger toys with more tactile interest.

# Developmental Milestones (months)

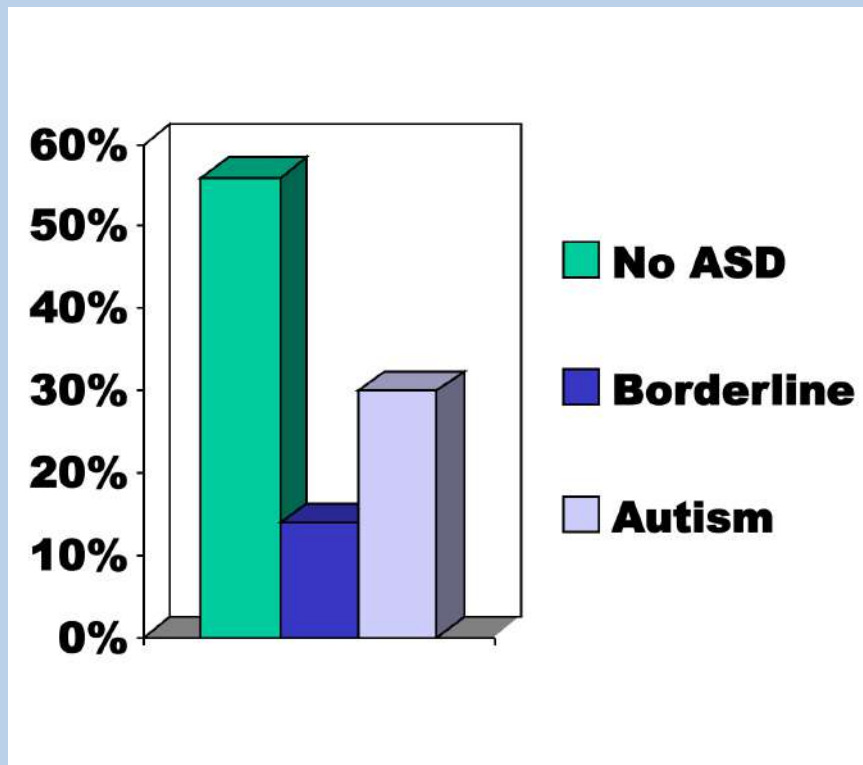
<b>Milestone</b>	<b>Norm</b>	<b>VI Only</b>	<b>VI +Autism</b>
Reaches/Touches Object	5.4	8.1	10.6
Sits alone	6.6	9.2	11.9
Crawls 3ft	9	11.4	18.3
Plays interactive game	9.7	9.3	13.1
Walks w/o support	13	19	26.6
Follows direction	20.5	19.3	25
Relates past experiences	40	36.9	37.7

# Research at CHLA

- Pilot study
  - ASD screening assessment added to prospective study
- Objective: Assess level of ASD
- Social-responsiveness scale (SRS)\*
  - performed at final study visit (age 5)

*\*modified for visual impairments*

# Social Responsiveness Scale- Results



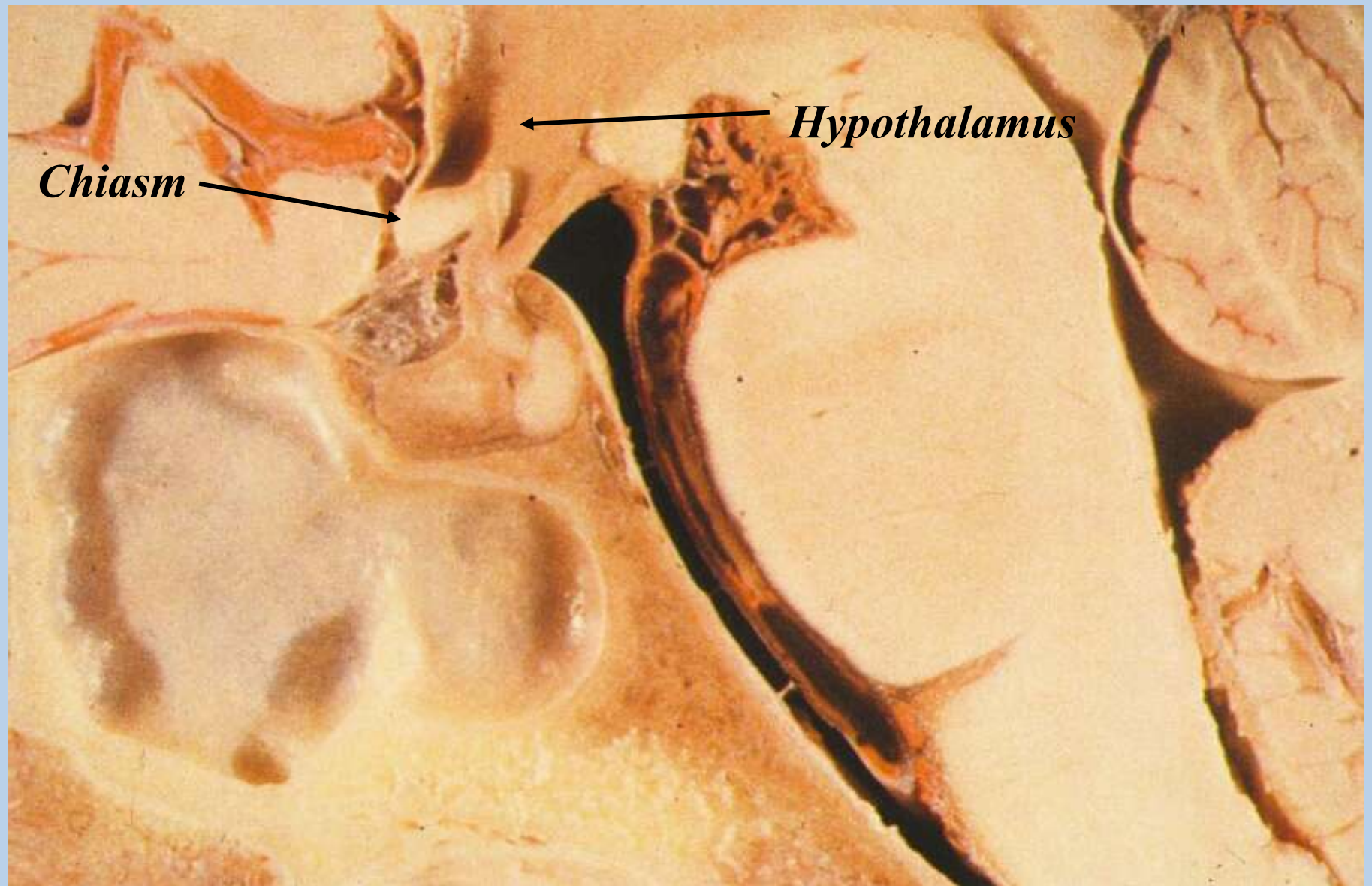
- 5/37 (13%) scored at the level of high-functioning ASD.
- 11/37 (30%) scored at the level of autism.

# Clinical Characteristics Associated with SRS

	High SRS	Low SRS
Corpus Callosum Hypoplasia	73%	40%
Seizures	36%	5%
Final Vision	Motion perception	20/80
Developmental Delay	90%	4.8%

# CHLA Study Autism Evaluations

- Aim: Modify existing ASD screening and diagnostic tools for use independent of vision.
- Evaluate participants (with and without signs of autism on the SRS) using the ADI-R and ADOS.





# *Signs of Hypothalamic Dysfunction*

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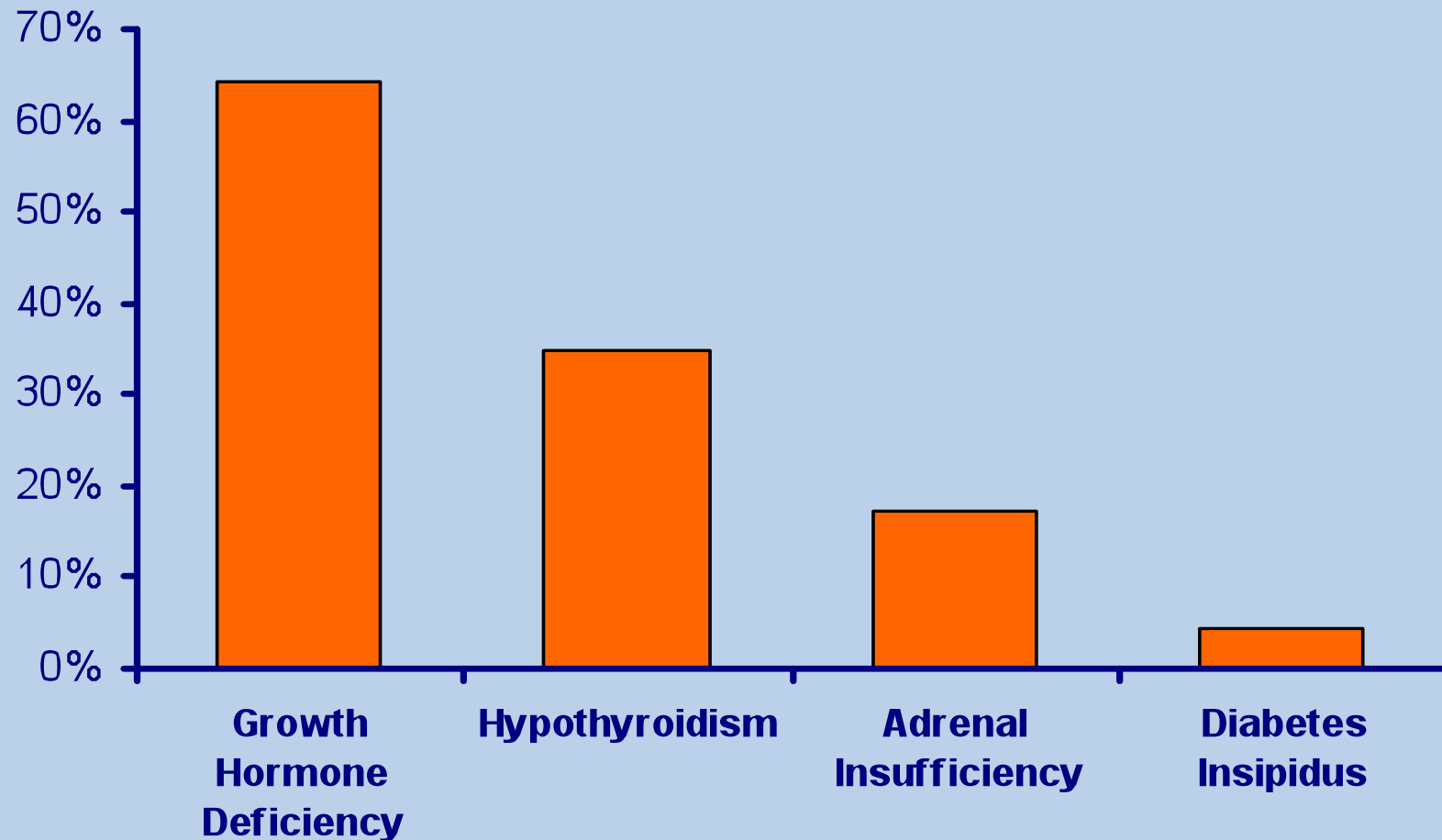
- Hypopituitarism
- Food or water seeking
- Obsessive-compulsive behavior
- Obesity
- Abnormal temperature regulation
- Circadian disorders

# *Hypopituitarism*

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- Deficiencies in:
  - Growth hormone
  - Thyroid hormone
  - ACTH (cortisol)
  - Anti-diuretic hormone (diabetes insipidus)
  - Sex hormones

## Frequency of Pituitary Hormone Deficiencies in Children with ONH



# *Corpus Callosum*

- Hypoplastic corpus callosum  
76% have endocrine dysfunction
- Normal corpus callosum  
70% have endocrine dysfunction

## *Septum Pellucidum*

- 39% missing the septum pellucidum  
2/3 have endocrine dysfunction
- 61% have the septum pellucidum  
3/4 have endocrine dysfunction

# *Endocrine Dysfunction & Developmental Delay*

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Any endocrine dysfunction

✓ 73.6% delayed (vs. 60% without dysfunction)

Hypothyroidism

✓ 93% delayed (vs. 51% with normal levels)

# *Newborn Thyroid Function*

- Thyroid hormone essential for brain development in infants
- Newborn screening (NBS) for primary hypothyroidism (1/3000) mandatory in U.S.
- High ( $>25\mu\text{IU}$ ) TSH reported by Calif. NBS
  - 94% sensitive for primary hypothyroidism
- Low TSH (associated with central hypothyroidism) not reported

# *Hypothyroidism & Vision in ONH*

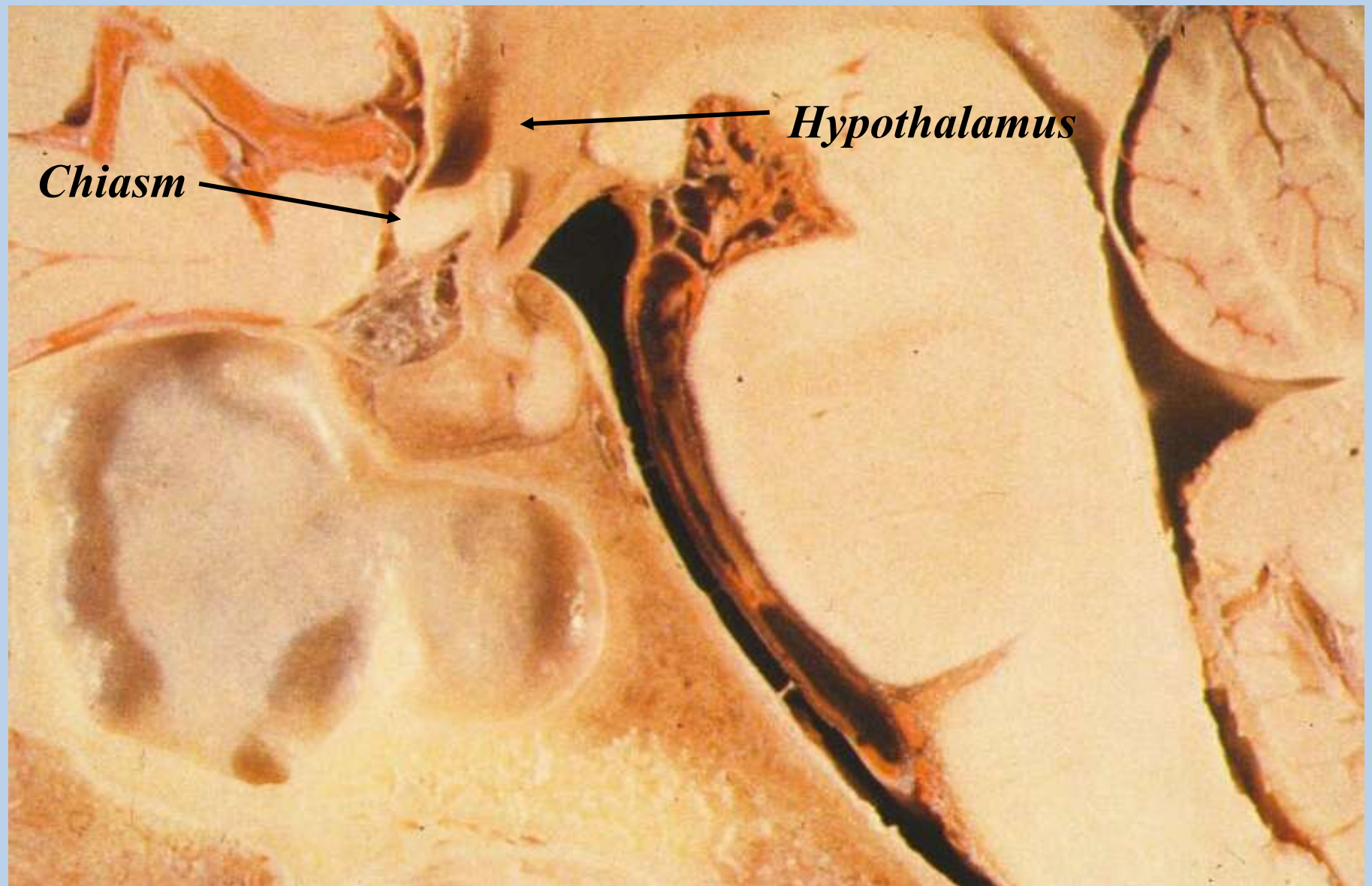
- Central hypothyroidism detected in ONH at mean age of 15 mos.
- Hypothyroidism is major risk factor for cognitive impairment in ONH
- Vision improves over 4-5 years in most children with ONH
- Thyroid hormone essential for optic nerve myelination in rodents



# *Laterality & Developmental Delay*

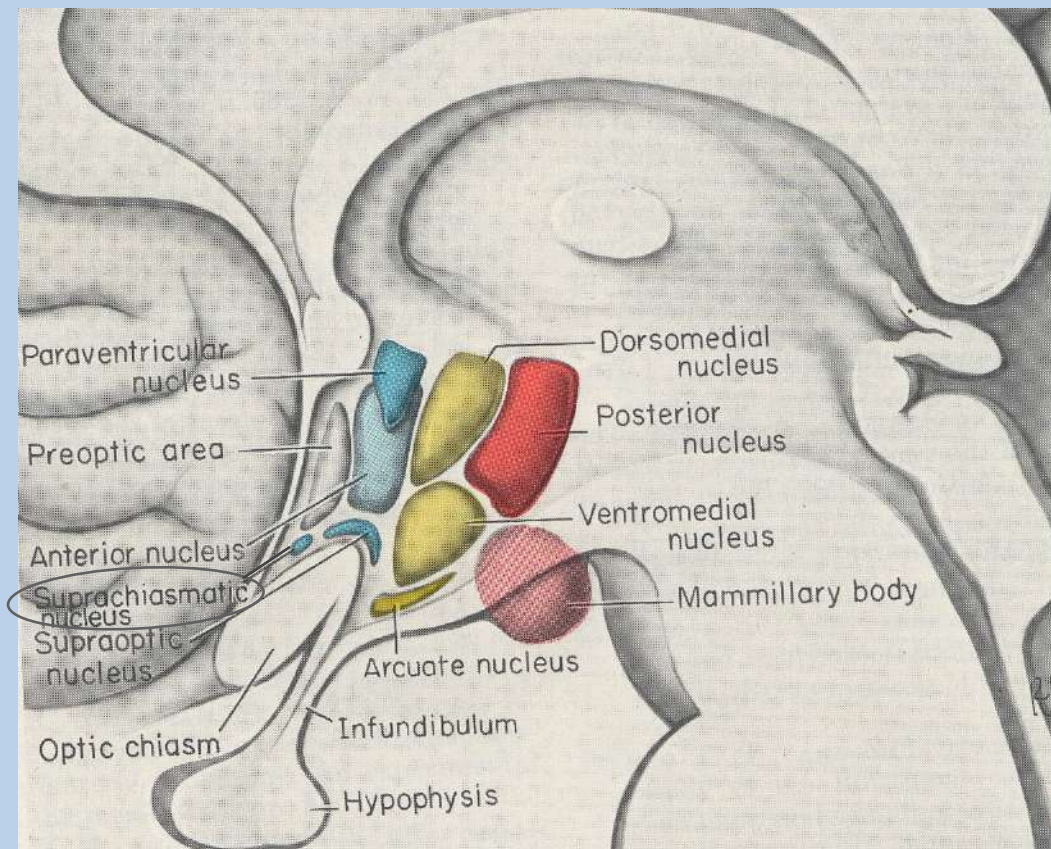
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- Unilateral cases (18%)
  - 38.5% have developmental delay
- Bilateral cases (82%)
  - 78.3% have developmental delay



# *Hypothalamus & Sleep Regulation*

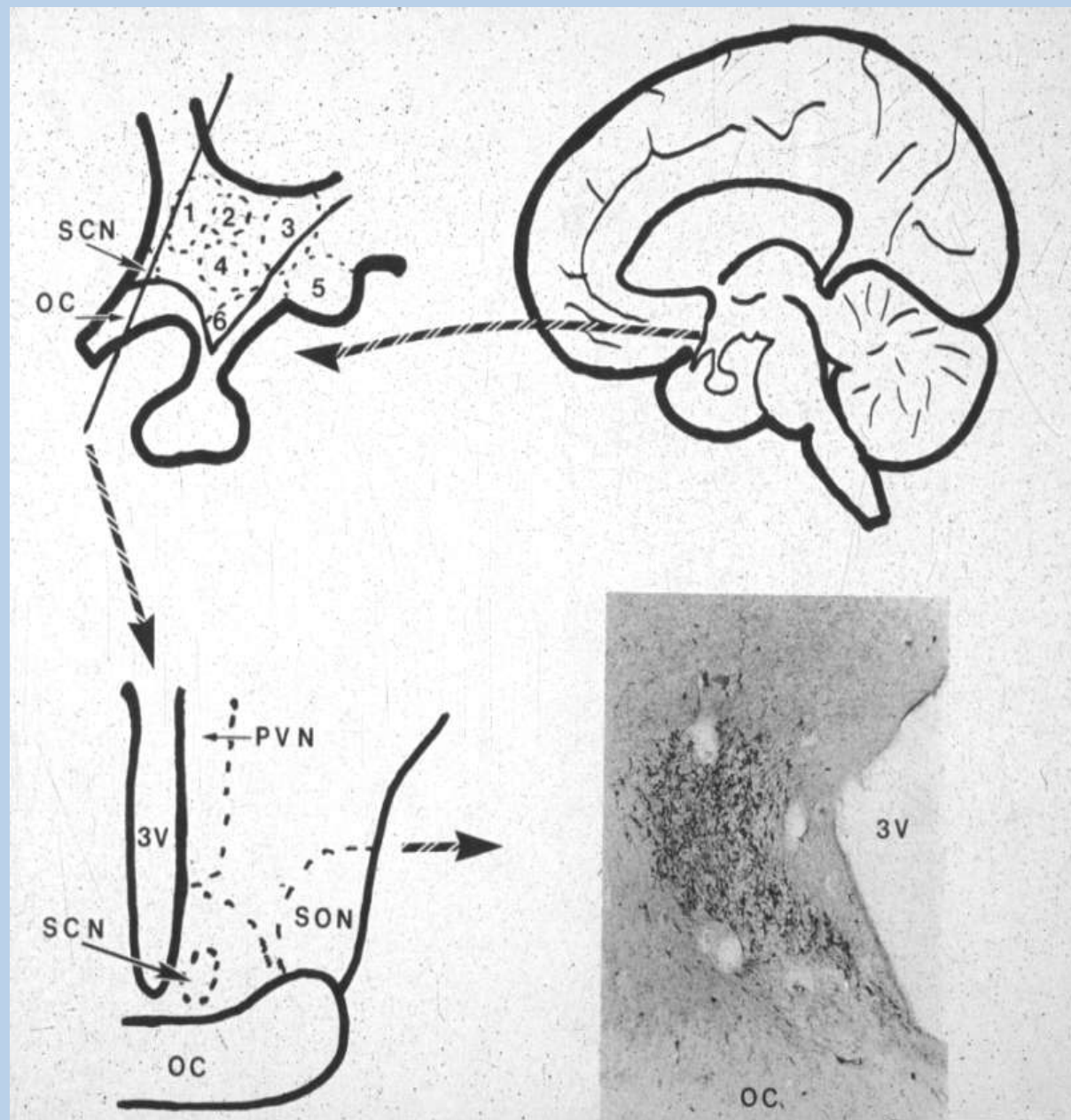
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## Suprachiasmatic Nucleus:

- Located in hypothalamus
- Controls circadian rhythms





# *Circadian Rhythm*

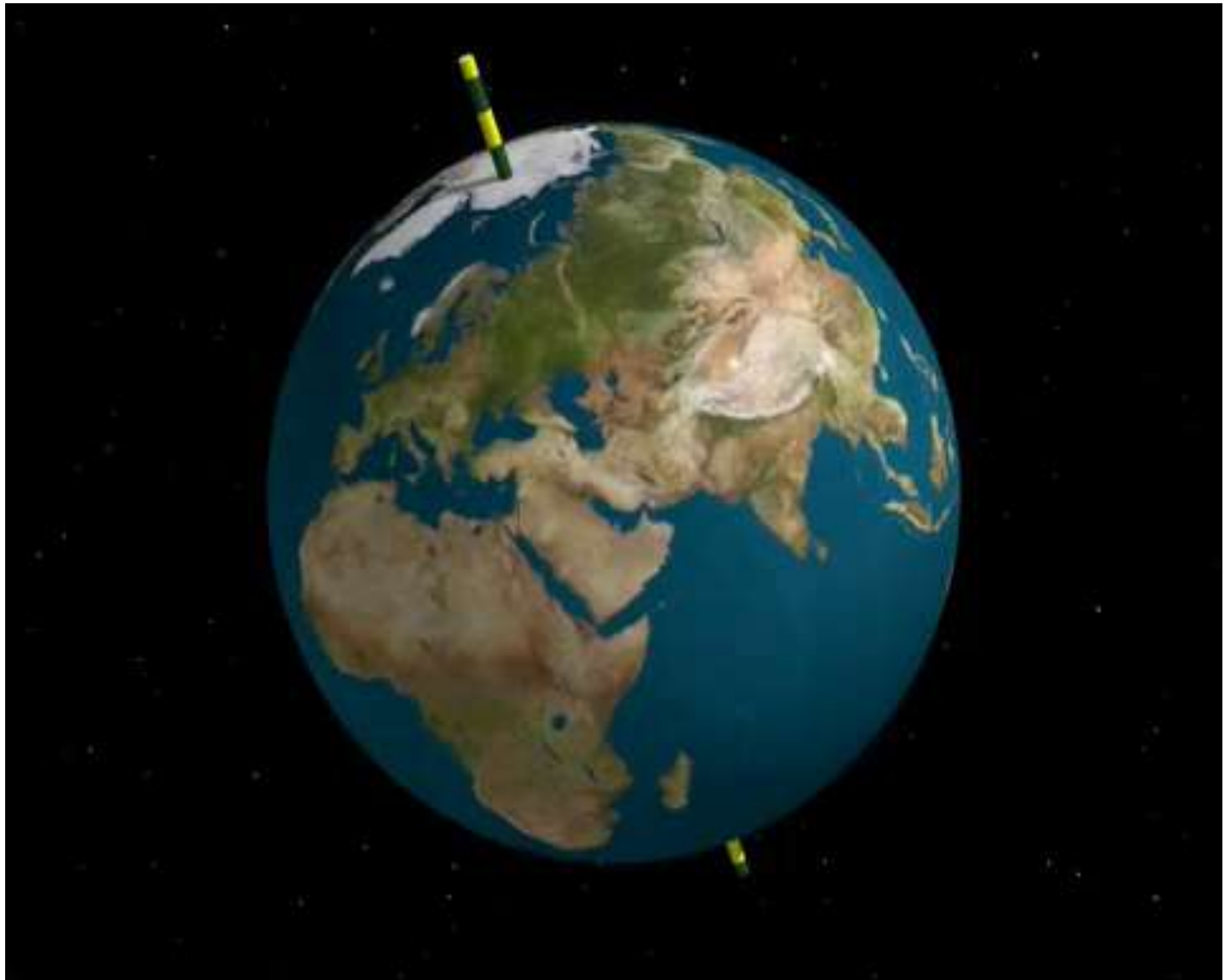
- Most cells of body have natural metabolic cycles.
- SCN neurons synchronize metabolic cycles of all cells approximately every 24 hrs.
- SCN suppresses release of melatonin from pineal gland.
- Melatonin suppresses brain and organ activity.

# *Circadian Rhythms*

- Endogenously generated
- Period of about 24.2 hrs
- Examples:
  - Temperature rhythms
  - Hormone rhythms
  - Sleep-wake cycles
- Must be entrained to the solar cycle

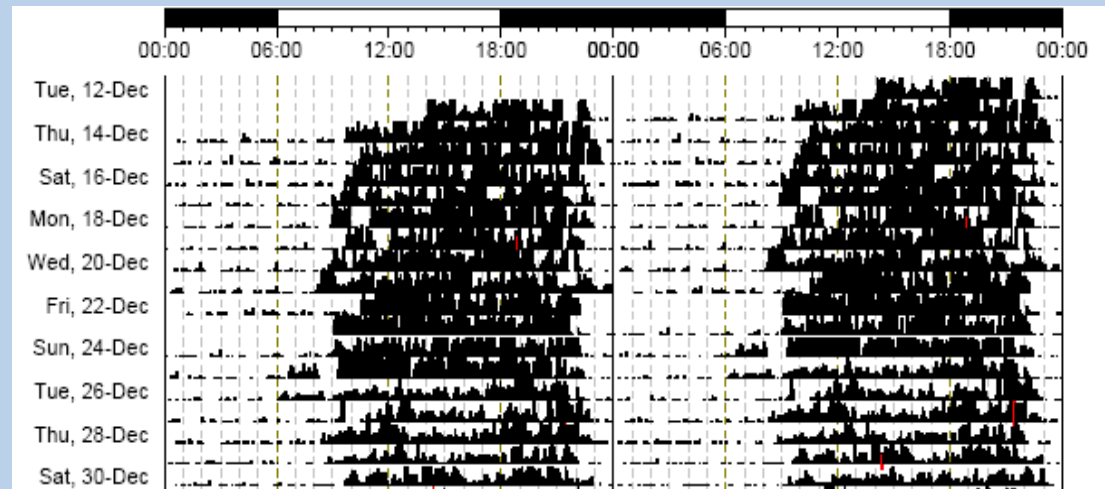
# *Circadian Entrainment*

- Triggered by light stimulating melanopsin ganglion cells in retina (especially blue light)
- SCN most susceptible to light entrainment just before and after temperature minimum (2-3 hrs before awakening)
- Examples:
  - Light exposure before T<sub>min</sub> causes later sleep next day.
  - Light exposure after T<sub>min</sub> causes earlier sleep next day.

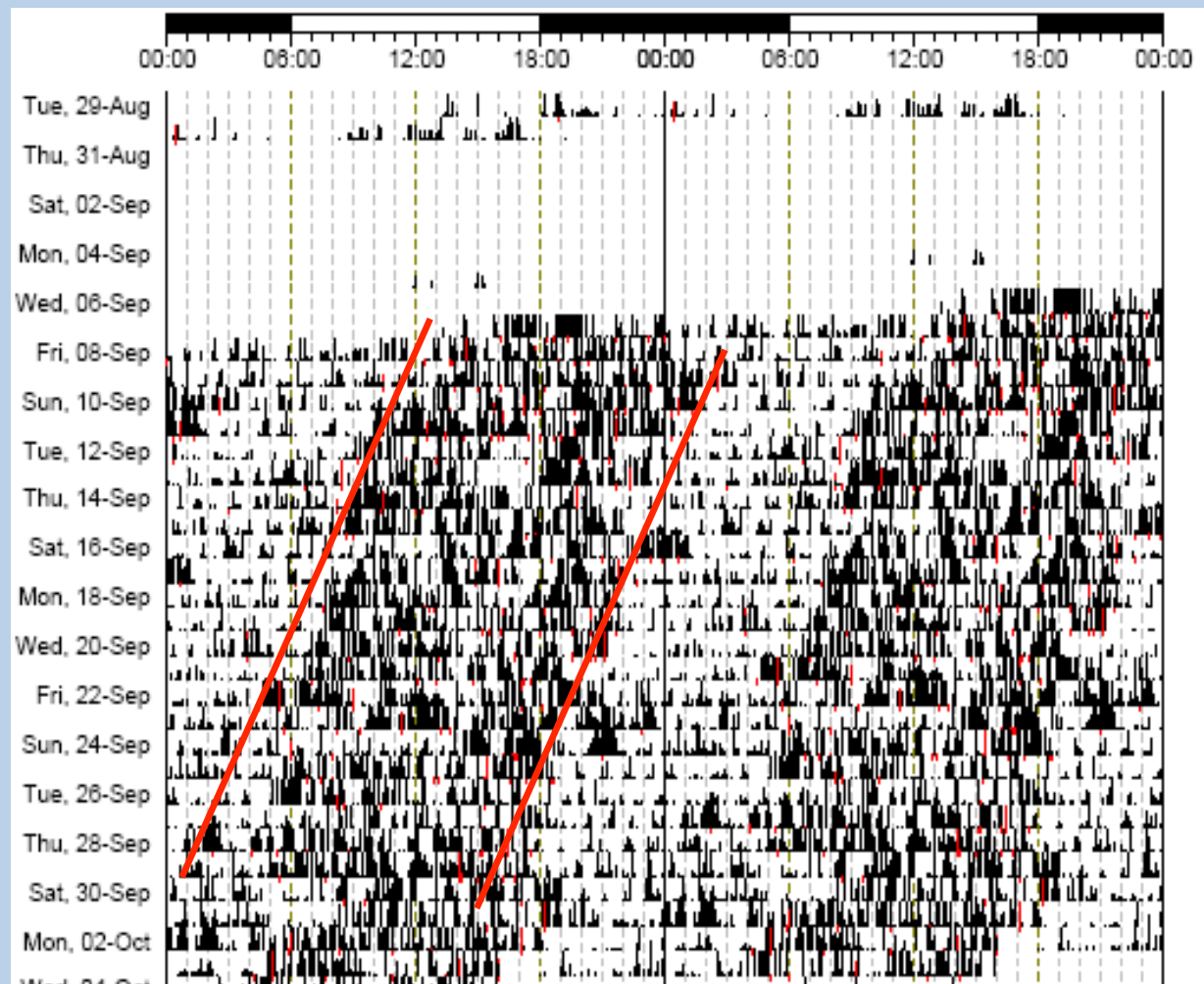




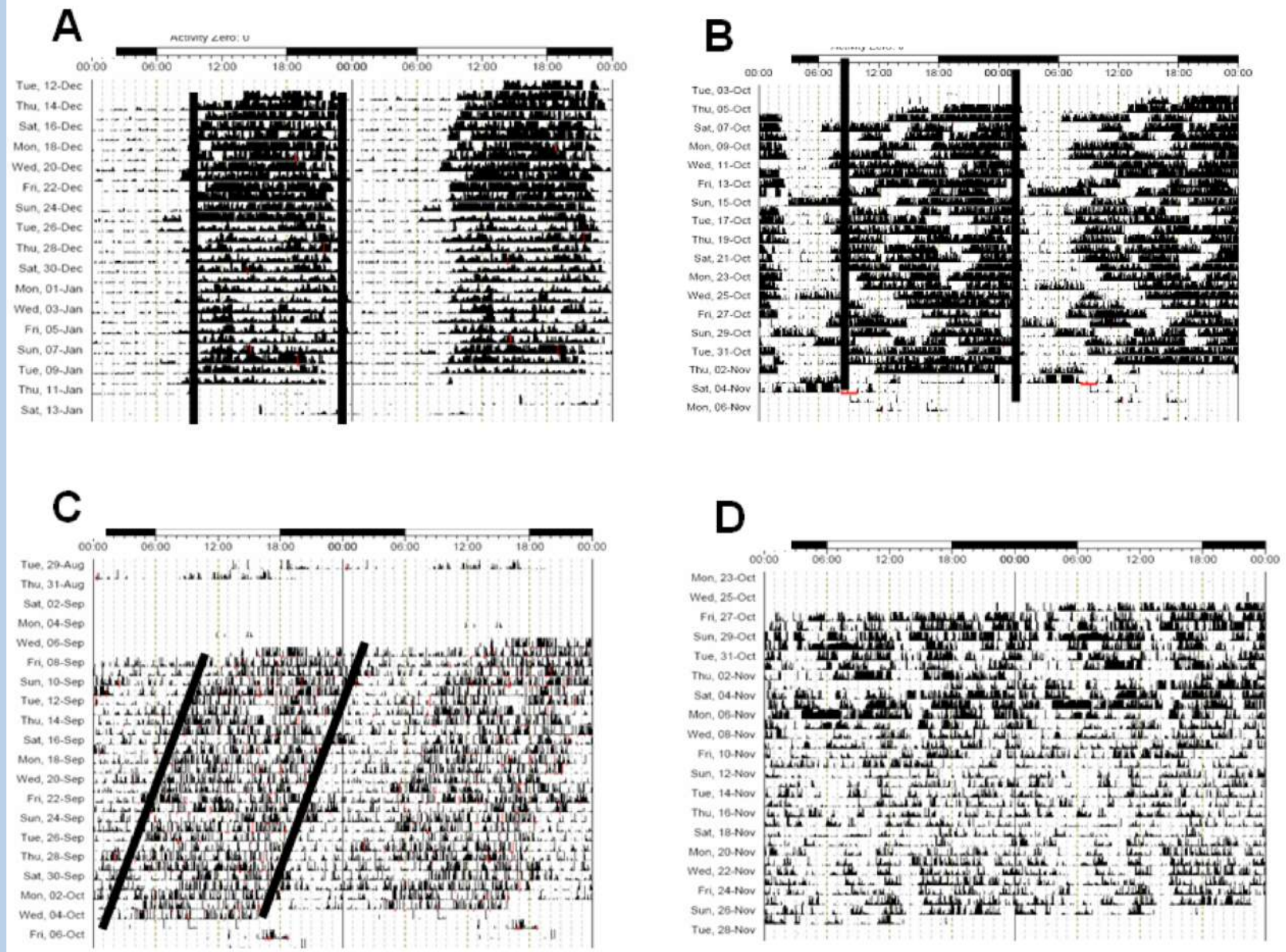
# *Actigraphy*



# *Free-running Sleep (no entrainment)*



# *Actigraphy in ONH*



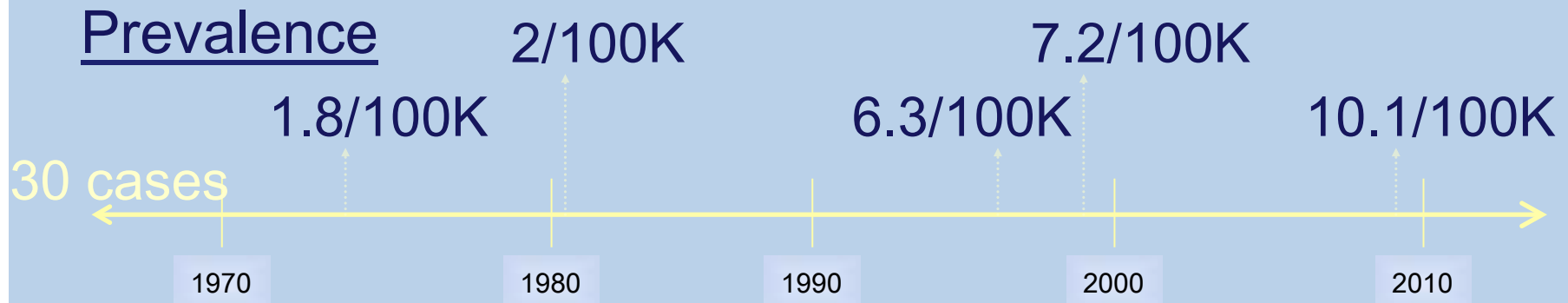
## *Clinical Associations with Sleep*

	Normal rest- activity	Abnormal rest- activity	P-value
# Subjects	13	6	
Age (mos.)	44	40	0.45
<b>Vision score</b>	1.7	4.7	<b>.006</b>
Normal pupils	85%	17%	.008
CC hypoplasia	30%	66%	0.18
≥1 hormone def.	53%	66%	>0.17
≥2 hormone def.	30%	66%	0.11
<b>≥3 hormone def.</b>	7%	66%	<b>.03</b>
<b>Dev. delay</b>	15%	100%	<b>.04</b>

## *General Observations*

- Most children with hypothalamic lesions and visual impairment have normal rest-activity patterns
- Daily activity patterns/environmental time cues sufficient to induce normal rest-activity patterns in many
- Optic Nerve Hypoplasia: Abnormal rhythmicity in 30%

# Optic Nerve Hypoplasia



## Leading cause of pediatric VI

Ireland

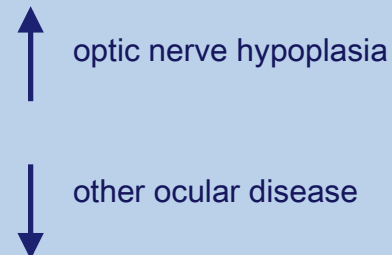
Scandinavia

United Kingdom

United States

## Childhood Vision Impairment Study <sup>†</sup>

Scandinavia: 1999 vs 1980



<sup>†</sup>Blohme et al. 2000



# Optic Nerve Hypoplasia

## Literature Review of Prenatal Risk Factors

- Very broad range of suggested prenatal correlates
- Previous research limited to
  - Anecdotal, case reports
  - Incidental findings from clinical research
  - Isolated epidemiologic reports
- Increasing interest in geographic clustering of cases

# Optic Nerve Hypoplasia

## Suggested Prenatal Correlates

### *Maternal factors*

- Young maternal age, primiparity are prominent maternal traits.

### *Prenatal exposures*

- Alcohol, drug use, and/or smoking is uncommon.
- Prenatal complications are infrequent.

### *Genetic factor*

- A mutation is unlikely.



# Optic Nerve Hypoplasia

## Geographic Clusters

- Anecdotal reports of spatial clusters
  - Geographic – isolated or near toxic point sources
  - Temporal – seasonal and annual
- 2006: U.K. report of clustering of cases at the time of diagnosis<sup>†</sup>
  - Disease events associated with factors of deprivation
    - Young maternal age, single, low education, unemployment

# Optic Nerve Hypoplasia

## What we know

- ONH is a leading cause of pediatric visual impairment.
- Young maternal age and primiparity are prominent features.
- The predisposing prenatal factors are unclear.

# Optic Nerve Hypoplasia

## Questions that Remain Unanswered

- What are the prenatal characteristics?
  - Frequency of the suggested correlates
  - Correlation of young maternal age with prenatal factors
- Do spatial-temporal clusters of ONH exist?
  - Association with population birth and socio-demographic factors

# Re-appraisal of Prenatal Risk Factors

- Design: Retrospective review of prenatal histories of a cohort of 204 cases (1995-20005)
- Analysis:
  - Maternal and prenatal characteristics
  - Comparison groups:
    - Maternal factors: 2000 national birth statistics
    - Prenatal factors: Compared to literature
- Findings: Some maternal features were verified and many refuted; and new potentially significant factors identified

# Re-appraisal of Prenatal Risk Factors

## Verified risk factors

- Young maternal age [ $23.5 \pm 6$  years (vs 27.2 yrs)]
- Predominance of primiparous mothers

Table 3. Infant and Maternal Characteristics at Birth

Category (N <sup>a</sup> )	n	%	2000 Birth Data (%)	p-value
Mother's Age at Birth (n=196)				
< 20	58	30	12	<0.001
20-24	71	36	25	
25-29	41	21	27	
30-34	16	8	23	
35-39	7	4	11	
40 +	3	2	2	
Parity (n=189)				
0	143	76	40	<0.001
1	32	17	32	
2	13	7	17	
3	1	1	6	

# Re-appraisal of Prenatal Risk Factors

## Verified risk factors

- Young maternal age and primiparity independent risk factors

Table 3a. Frequency of Primiparity (n=188)

Age Category	Primiparity (%)		p-value
	ONH	National	
< 20	96	79	<0.001
20-24	80	46	<0.001
25-29	59	36	<0.001
30-34	50	29	0.14
35-39	57	22	0.05
40 +	0	21	0.07

Primiparous mothers: 22 years (vs 24.9 yrs)

# Re-appraisal of Prenatal Risk Factors

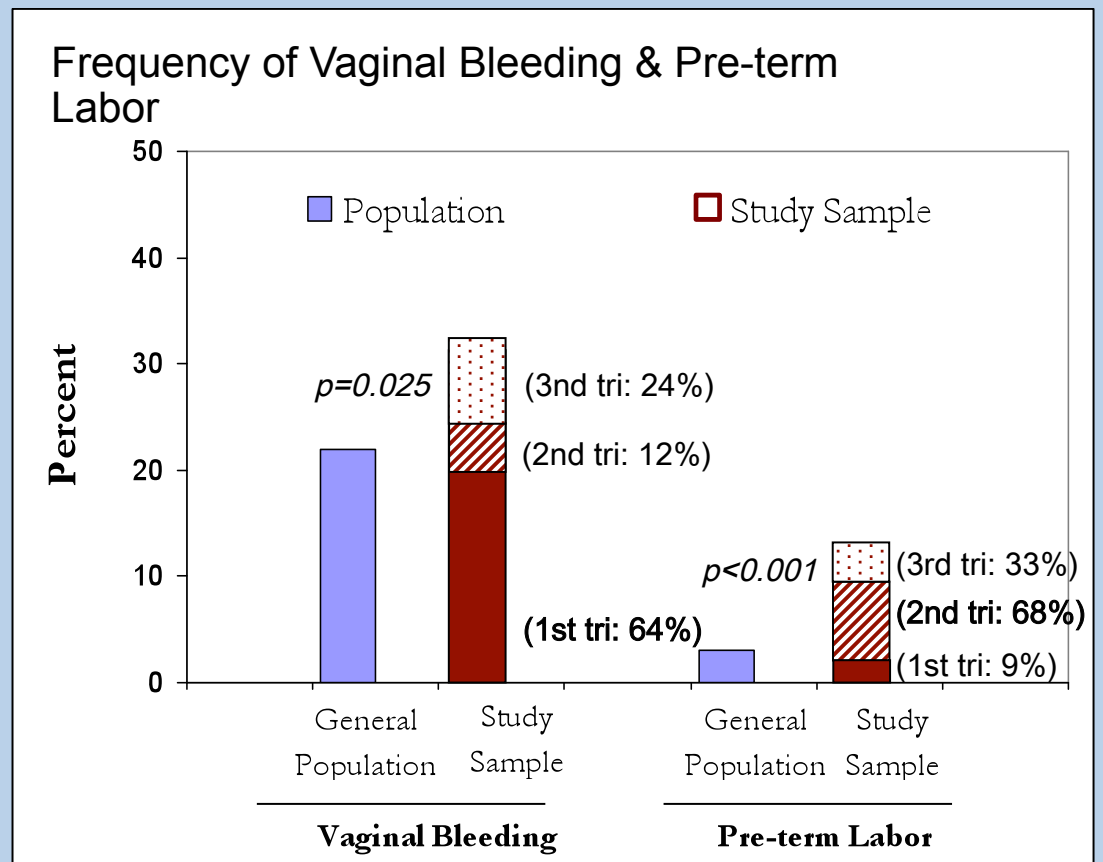
## Refuted risk factors

- Hypertension, diabetes, and viral infections
- Alcohol use
- Drug use
- Smoking

# Re-appraisal of Prenatal Risk Factors

## New potentially significant correlates

- Vaginal bleeding
- Pre-term labor





# Re-appraisal of Prenatal Risk Factors

## New potentially significant correlates

- Low weight gain
- Weight loss

Table 5a. Pre-pregnancy BMI and low weight gain during pregnancy<sup>†</sup>

BMI Categories	% Low Wt Gain		p-value	Recommended Wt Gain <sup>†</sup> (lbs)	Average Wt Gain <sup>a</sup>
	ONH	Pop.			
Low (<19.8)	35	3.7	<0.001	28	20 ± 5.2
Normal (19.8-26)	28	5.3	<0.001	25	16.5 ± 5.9
High (>26)	24	-		11	-5 to -41 lbs

<sup>†</sup> According to Institute of Medicine (IOM) (1990) guidelines.

<sup>a</sup> Among subjects that reported low weight gain.

# Re-appraisal of Prenatal Risk Factors

## New potentially significant correlates

- Low weight gain
- Weight loss

Table 5b. Weight Loss

Category	n	%
Any weight loss	50	48
In 1 <sup>st</sup> or 2 <sup>nd</sup> trimester	45	91
Weight loss of 5+ pounds	33	31

- Weight loss more common with decreasing age
- 22 years vs 26 years;  $p=0.002$

# Re-appraisal of Prenatal Risk Factors

## Summary

- Young maternal age & primiparity persist as correlates
- Many previously suggested risk factors are uncommon
- A high frequency of
  - Vaginal bleeding and pre-term labor
  - Low weight gain and weight loss

# Optic Nerve Hypoplasia

## Questions that Remain Unanswered

What is the prenatal history associated with ONH?

- What are the prenatal characteristics?
  - Frequency of the suggested correlates
  - Correlation of young maternal age with prenatal factors
- Do spatial-temporal clusters of ONH exist?
  - Association with population birth and socio-demographic factors

# ONH Clustering Analysis

## Research Plan

Analyze geographical data of the prenatal period for cases of ONH

- Mother's residential location during the prenatal period
- Time period of interest: 1<sup>st</sup> trimester

Preliminary step to direct future research, including cluster validation

*Proposal funded by: Prevent Blindness in America (2010-2011)*

# ONH Clustering Analysis

## Study Design

- National registry of cases of ONH within the United States
- Retrospective cohort of cases of ONH
- Data collection
  - Birth season & year
  - Mother's residential location: 3-months prior to conception, during 1<sup>st</sup> trimester, and during the 2<sup>nd</sup> trimester
  - Geographical data aggregated to the zip code level

# ONH Clustering Analysis

## Inclusion criteria:

- Reported diagnosis of ONH
- Knowledge of maternal residential location during pregnancy

## Recruitment:

- Cases of ONH identified from early intervention programs
- Study availability notices distributed quarterly to service providers
- Survey provided to families to complete on-line or by mail



## SECTION 1

When was your child born? (Please only use season and year.)

Season

Fall = September, October, November    Spring = March, April, May  
Winter = December, January, February    Summer = June, July, August

Year

Where did you live 3 months before you became pregnant with your child that was diagnosed with ONH?

A.

Zipcode

OR

B. Block Number  
& Street Name

Block number example:

1826 Street Name

1800 is the block number

City or County

State

Where did you live during the first 3 months of your pregnancy?

A.

Zipcode

OR

B. Block Number  
& Street Name

Block number example:

1826 Street Name

1800 is the block number

City or County

State

Where did you live between the 3rd and 6th months of your pregnancy?

A.

Zipcode

OR

B. Block Number  
& Street Name

Block number example:

1826 Street Name

1800 is the block number

City or County

State





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### **Section 3**

#### **Contact Information**

The results of this survey will help provide a picture of how ONH is distributed. It is possible that new surveys or research studies will develop from these results. If you would be interested in participating in future research and would like to be contacted, please provide your current contact information in the space provided below. You are not required to provide this information for participation in this survey. This is completely VOLUNTARY.

State and federal privacy laws protect the use and release of your information. The contact information that you provide is considered protected health information. Under these laws, the study directors cannot use your contact information unless you give permission. If you decide to give your contact information, this will indicate that you give permission for Dr. Mark Borchert and/or Pamela Garcia-Filion to use your information to contact you in the future for the purpose of research. Your choice about whether or not to participate will have no effect on any future access for you or your child to care, services or benefits at Childrens Hospital Los Angeles.

Your name and contact information will be kept in a private database and only be used to contact you if it is determined that your information will be useful for future research. It will not be provided to other researchers, put into a research report or used to receive compensation.

This information will only be used by Dr. Mark Borchert and Pamela Garcia-Filion for this research study. However, your information may also be seen by the CHLA Institutional Review Board and U.S. government agencies that are required by law to review and monitor research activities.

This permission to release your contact information to the research investigators will expire when the research study ends. At that time, all contact information will be destroyed. You can print a copy of this survey and privacy protection statement for your records. You can cancel your permission at any time by writing to Dr. Mark Borchert and request that your information be removed. If you cancel your permission, information that was already collected and disclosed about you may continue to be used. Please feel free to call the CHLA Institutional Review Board [(323) 669-2265] or Dr. Mark Borchert [(323) 669-4510] with any questions about the privacy of your contact information.

#### **Full Name of Parent:**

#### **Current Contact Information:**

Street Address

City

State

Zipcode

Phone Number

Submit

Reset

# *National On-line Survey*

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- [www.onesmallvoicefoundation.org](http://www.onesmallvoicefoundation.org)
- [www.onhsurvey.org](http://www.onhsurvey.org)

Thank you