Optic Nerve Hypoplasia

ChildrensHospitalLosAngeles
International Leader in Pediatrics

KECK
SCHOOL OF MEDICINE USC

Mark Borchert M.D.

- 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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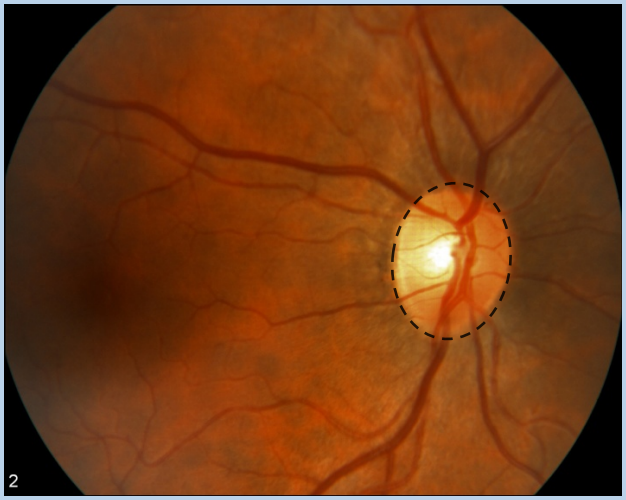
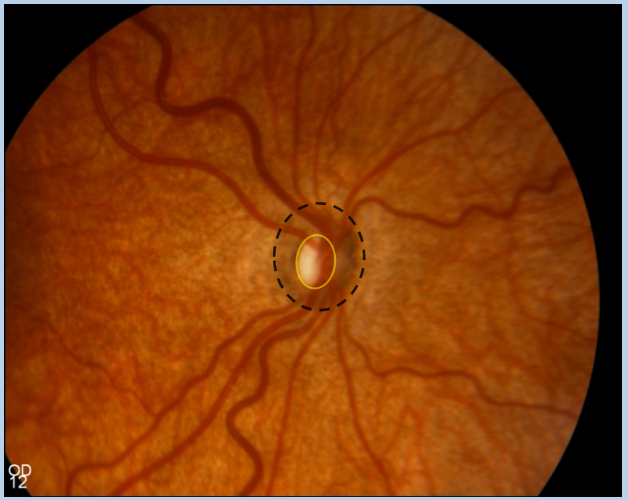
and by
One Small Voice Foundation

Optic Nerve Hypoplasia

Definition: Underdeveloped optic nerve in one or both eyes





Birth defect estimated to occur between 7th & 15th gestational week

Pathogenesis of ONH

- 1st 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. *Albrecth 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 (Neurological) of the University of Southern California

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 Tenchini (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 postencephalitic 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.

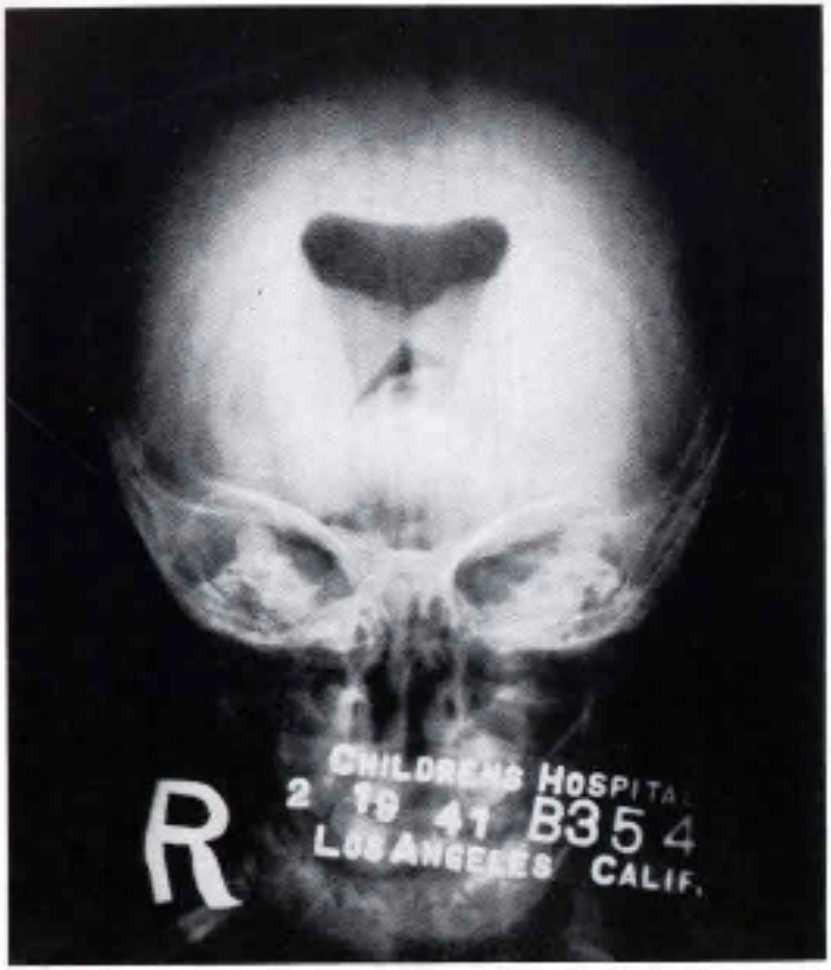


FIG. 2. ENCEPHALOGRAM. ANTEROPOSTERIOR VIEW SHOWING MEDIAL CONFLUENCE OF THE LATERAL VENTRICLES ANTERIORLY RESULTING FROM ABSENCE OF THE SEPTUM PELLUCIDUM

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[1]). 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 ½, 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.

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[1]) *Morsier, G. de:* Etudes sur les dysraphies crânio-encéphaliques: I. Agénésie des lobes olfactifs (télencéphaloschizis latéral) et des commissures calleuse et antérieure (télencéphaloschizis 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 (rhomboschizis). Mschr. Psychiat. Neurol. 1955, 129, 321–344.

Schweizer Archiv fur Neurologie und Psychiatrie 1956, 77:267–292.

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?

Definition: Underdeveloped optic nerve

Clinical Associations:

- Brain Malformations
- Developmental Delay
- Hypopituitarism
- Vision Impairment

Isolated ONH is uncommon

CHLA Research Program

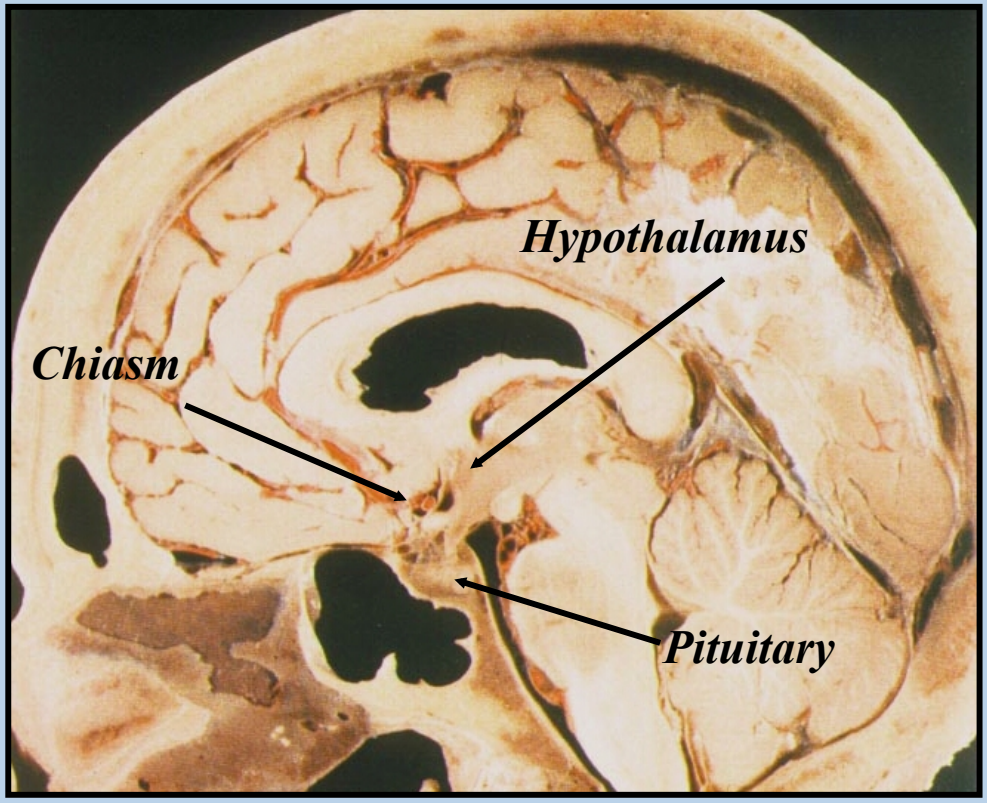
- Pathology
- Clinical Studies
  - Prospective observational
  - Intervention trials
- Epidemiologic investigations
  - Disease distribution in U.S.
  - Etiology

CHLA Prospective ONH Study

Children ≤ 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



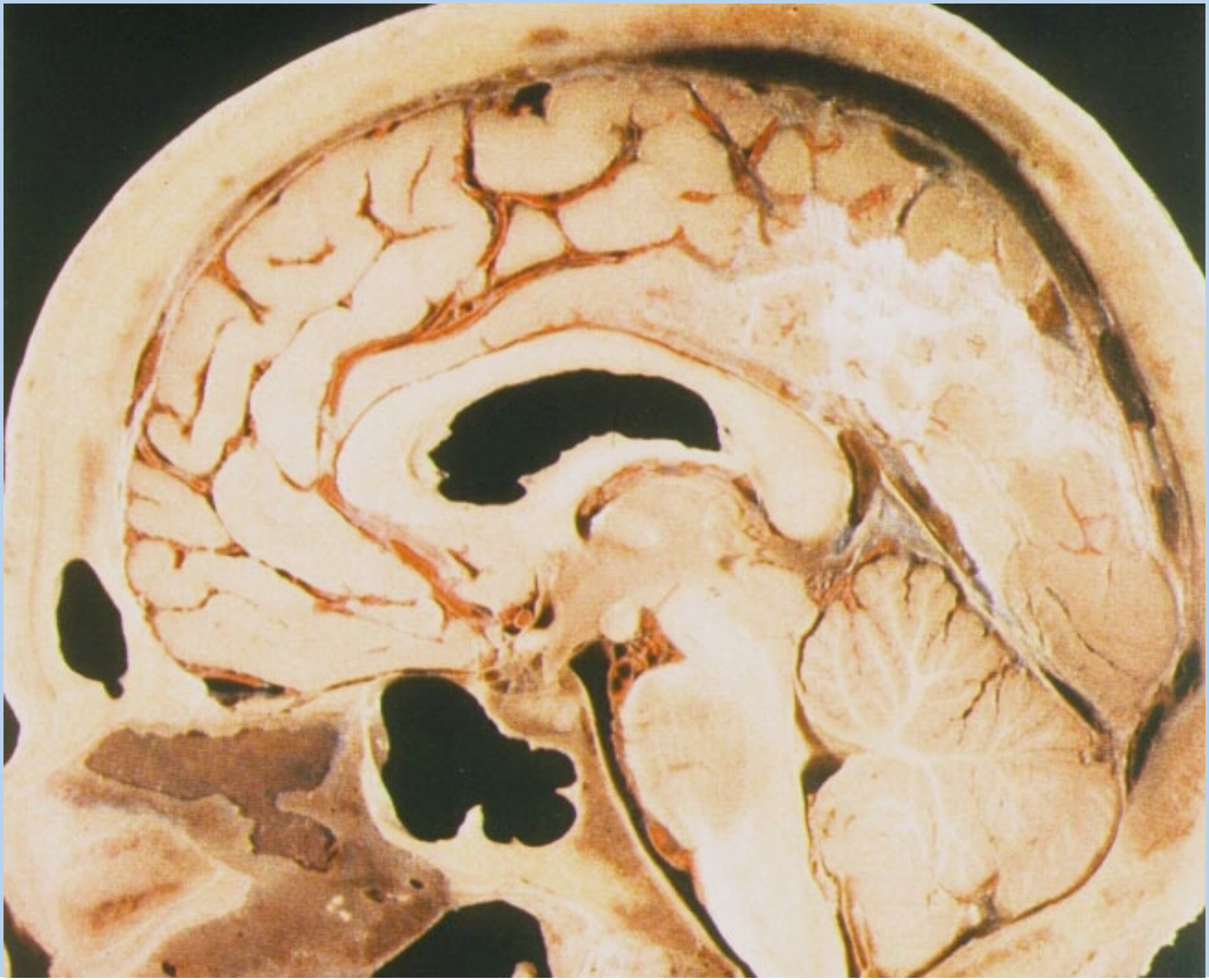
CNS Abnormalities in ONH

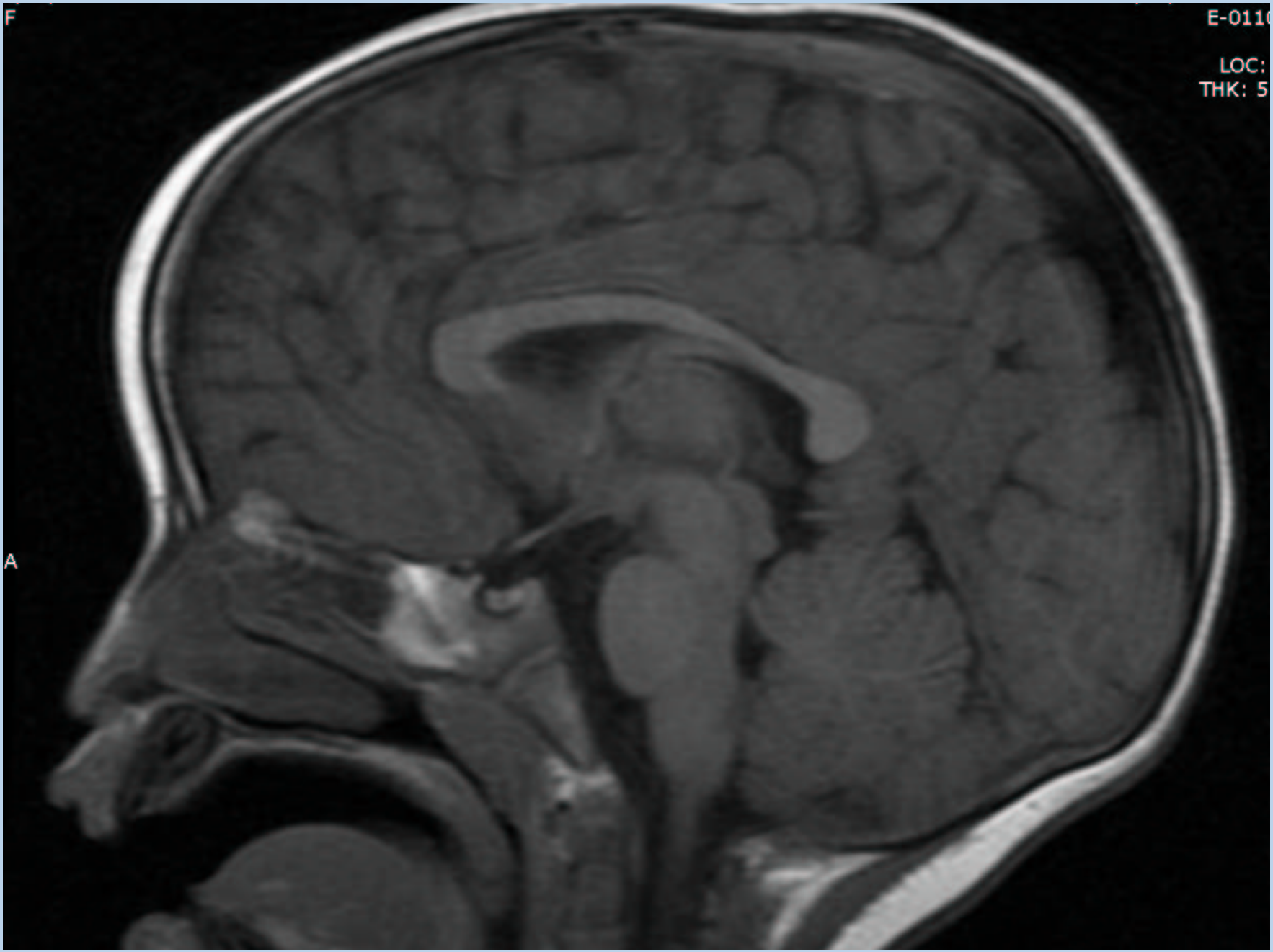
- Hypoplasia of corpus callosum 38%
- Absence of septum pellucidum 38%
- Pituitary dysgenesis 13%
- Other major malformations 14%
  - hydrocephalus
  - white matter hypoplasia
  - micropolygyria
  - schizencephaly

- *Based on first 73*

MRI Findings & Developmental Delay

- 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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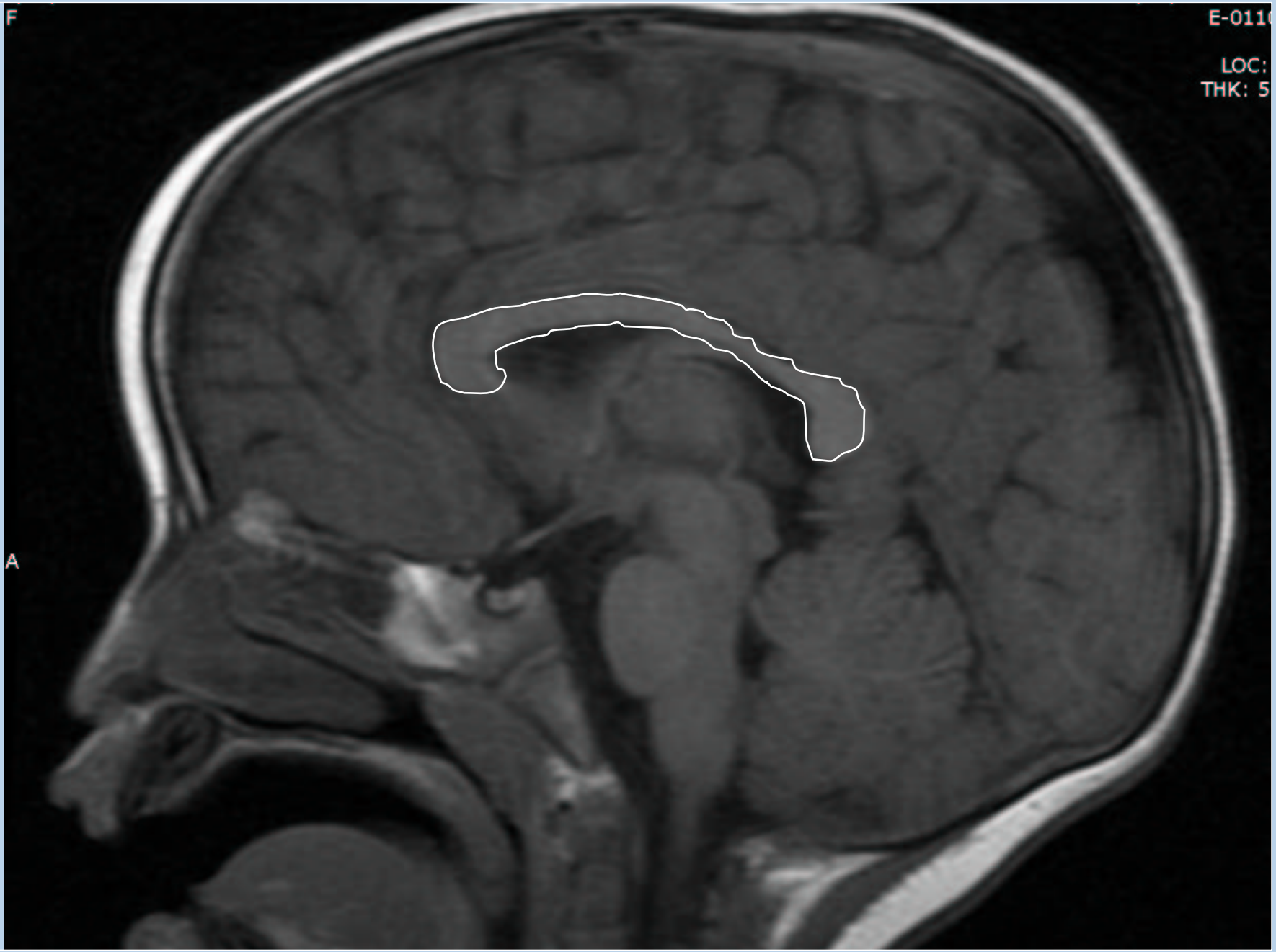
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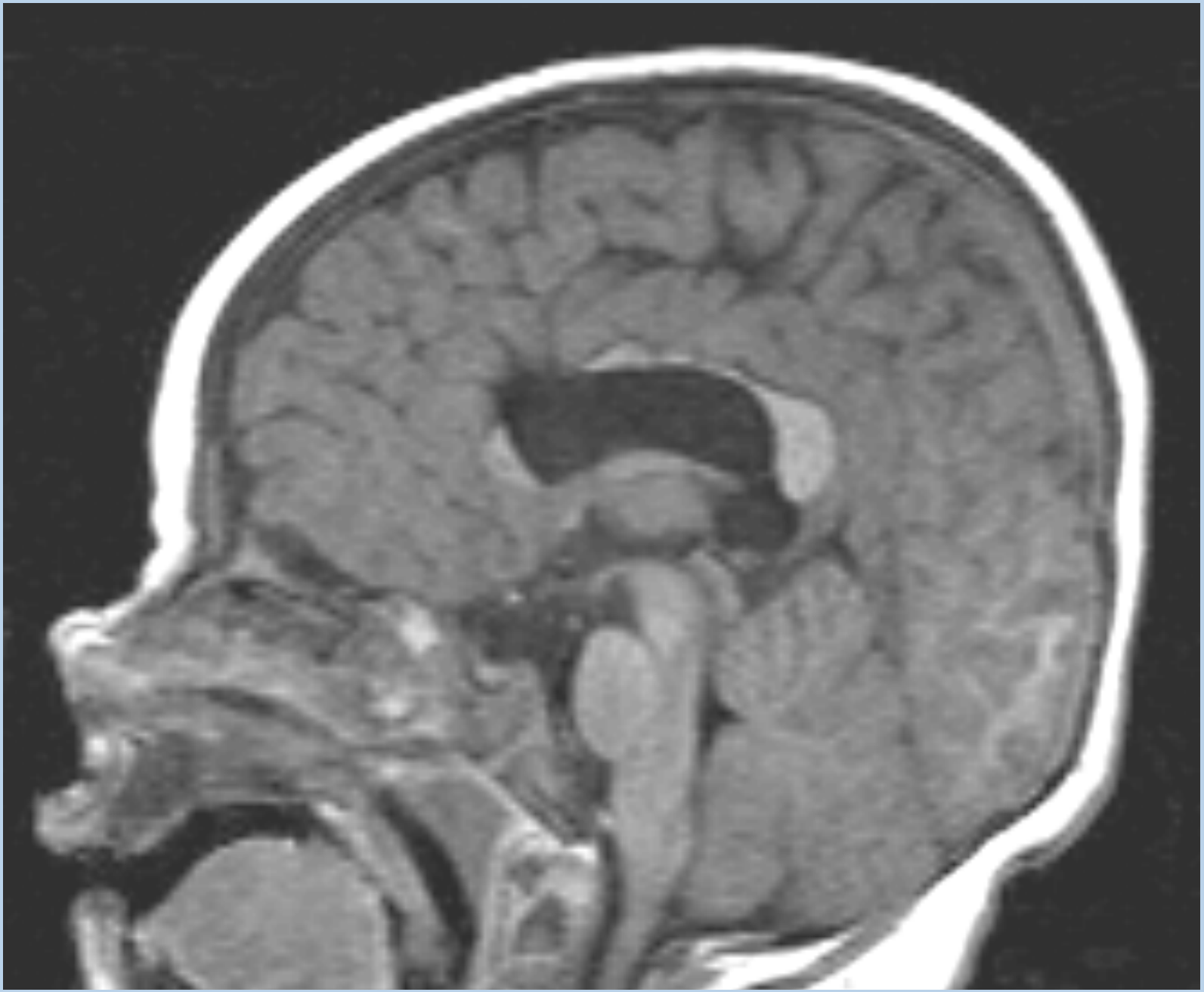

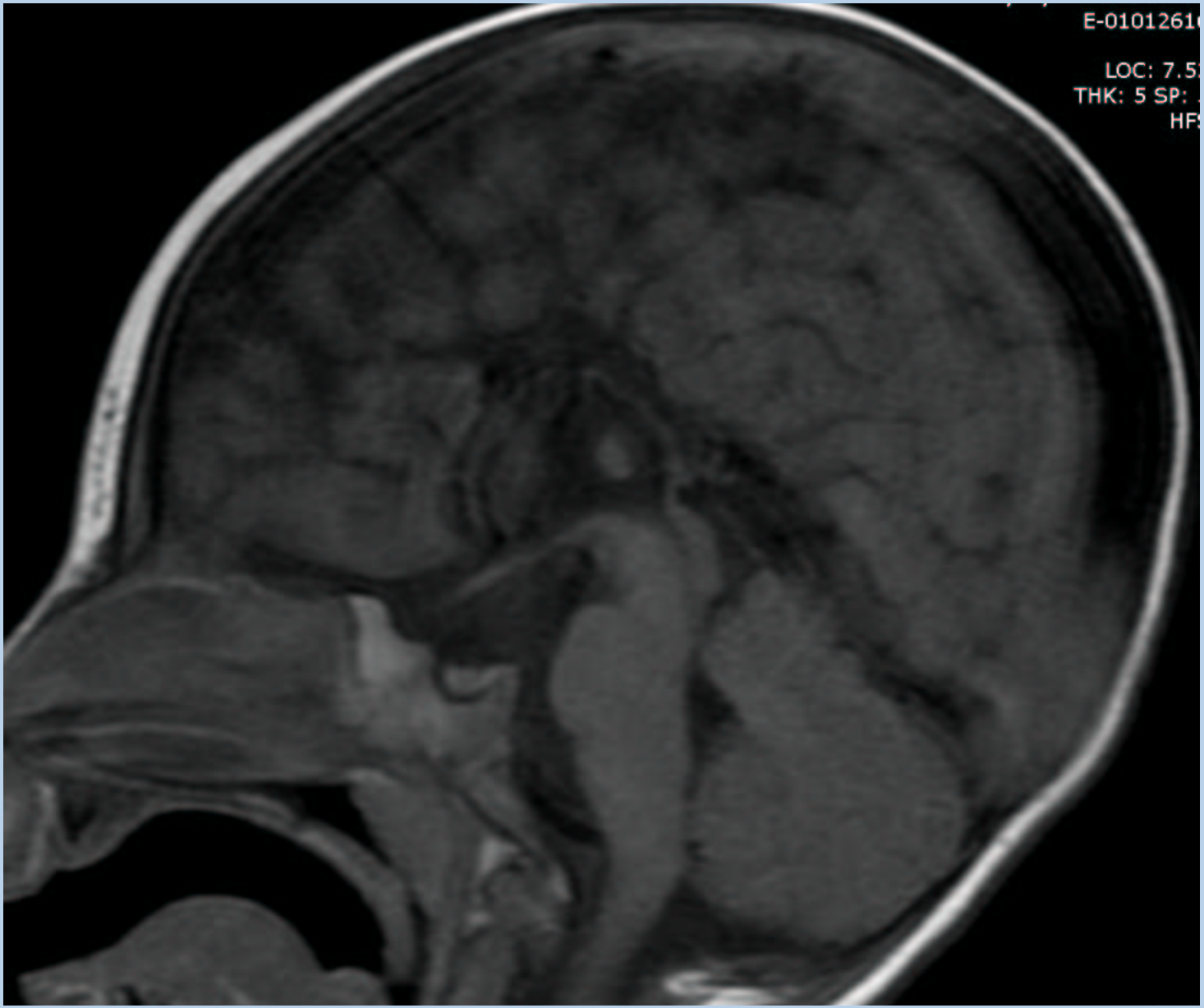
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Corpus Callosum and Developmental Disorders

- 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

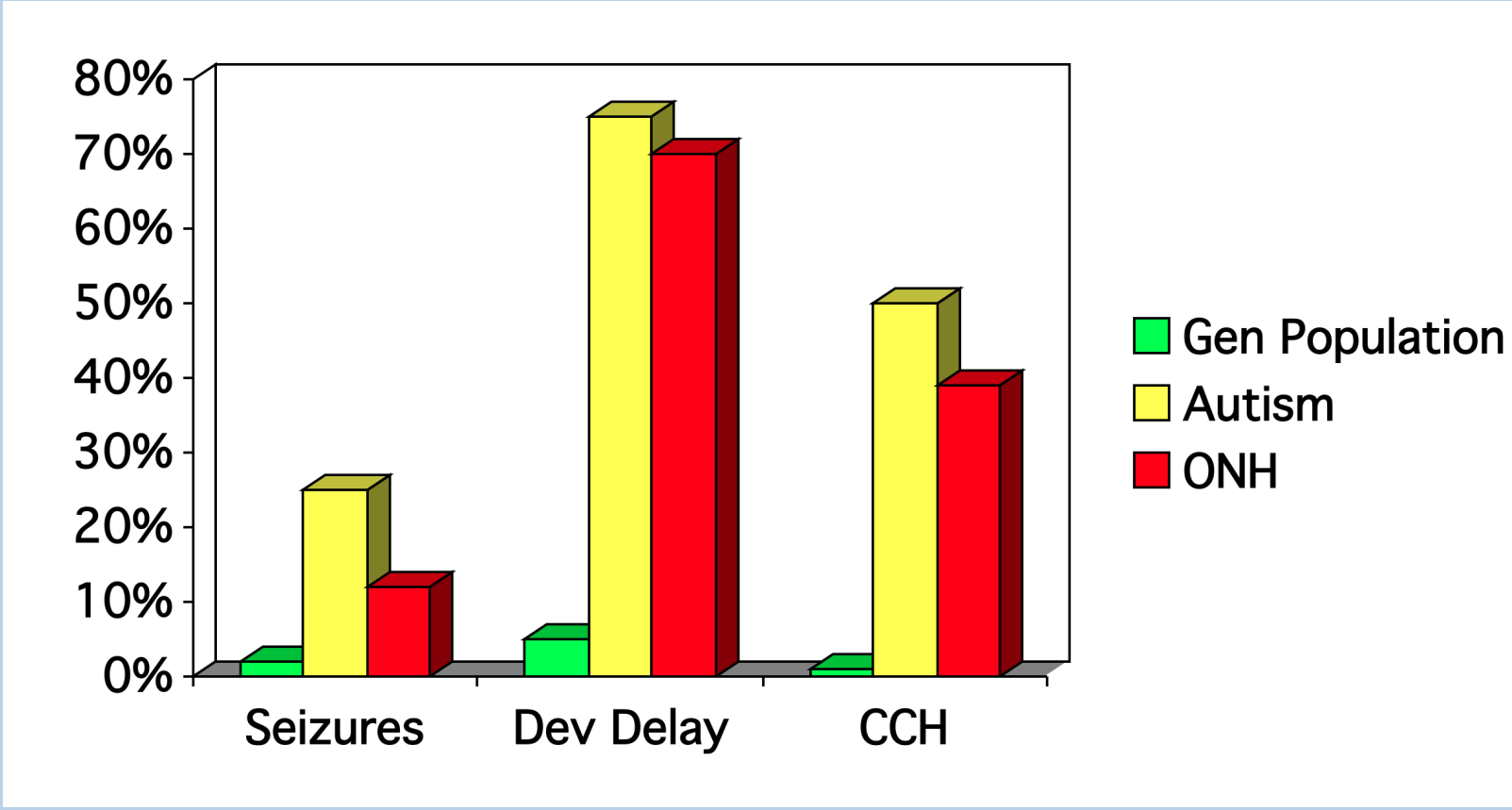
Autism noted in ONH

- 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

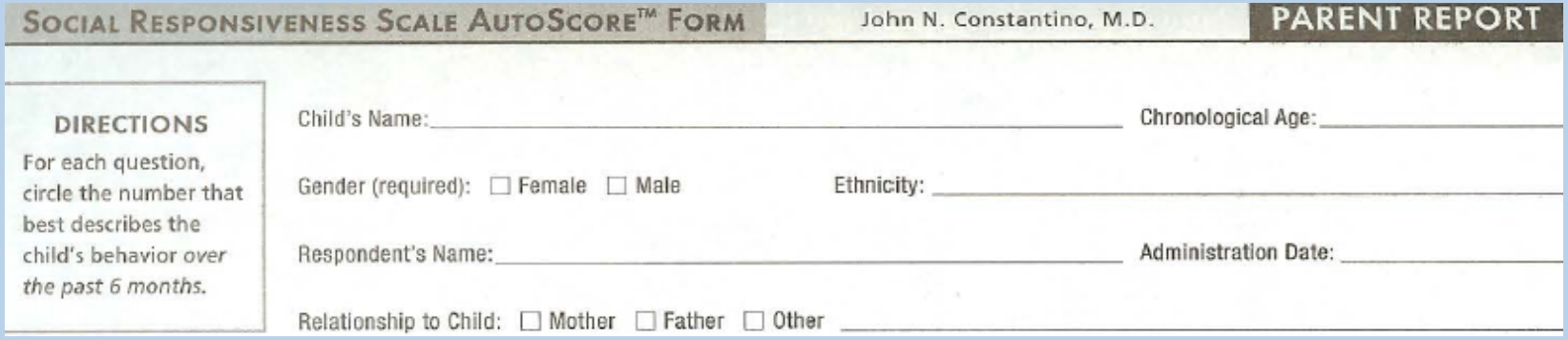


Question: Is this behavior really autism?

- 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)



SOCIAL RESPONSIVENESS SCALE AUTOSCORE™ FORM | John N. Constantino, M.D. | PARENT REPORT

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)

Milestone	Norm	VI Only	VI +Autism
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

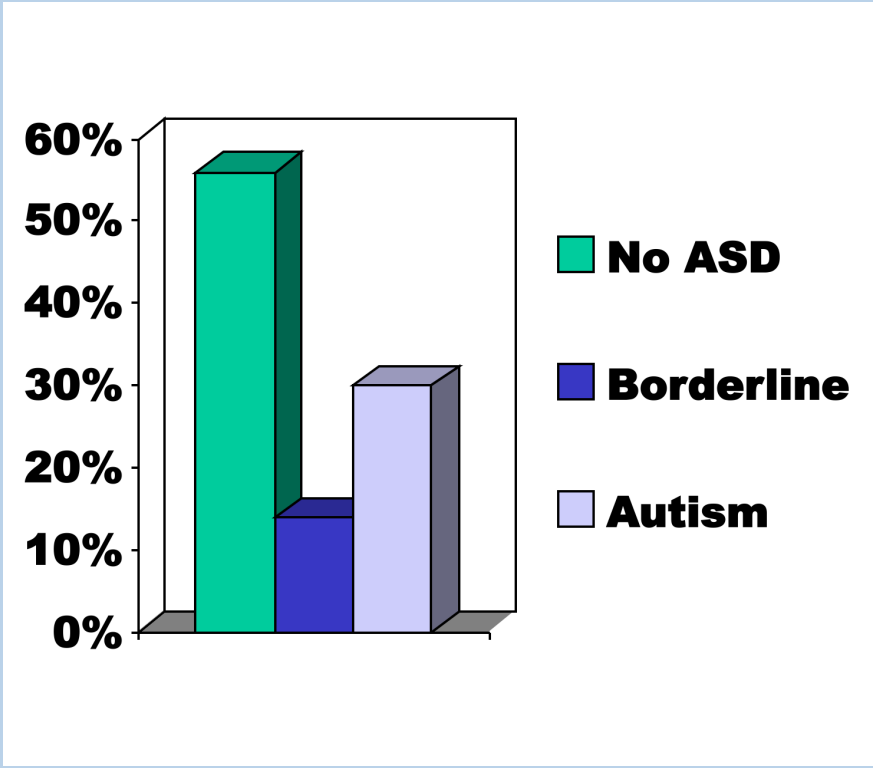
- Pilot study

→ 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



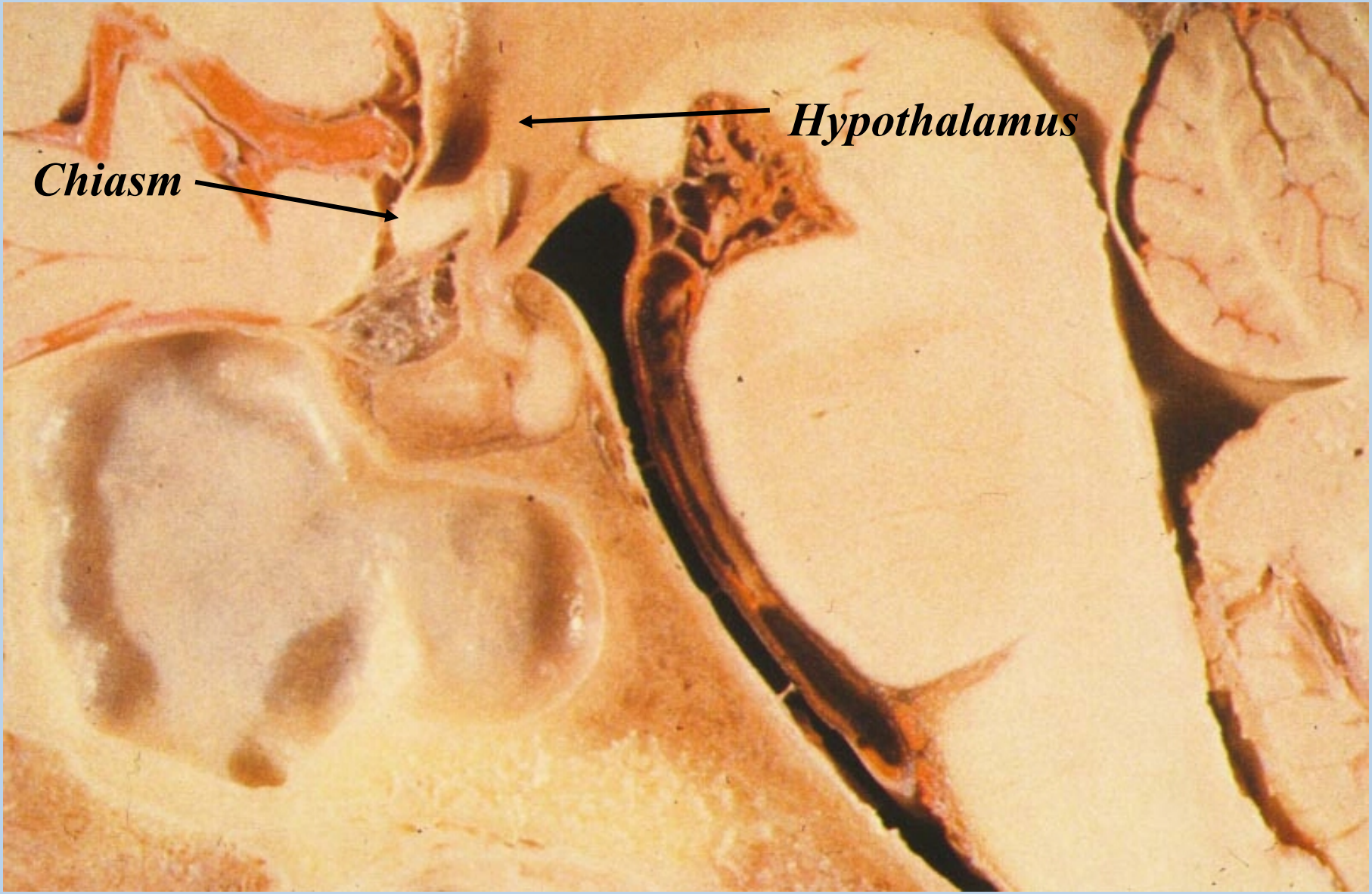
- 5/37 (13%) scored at the level of high-functioning ASD.
- 11/37 (30%) scored at the level of autism.

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.


Hypothalamus
Chiasm

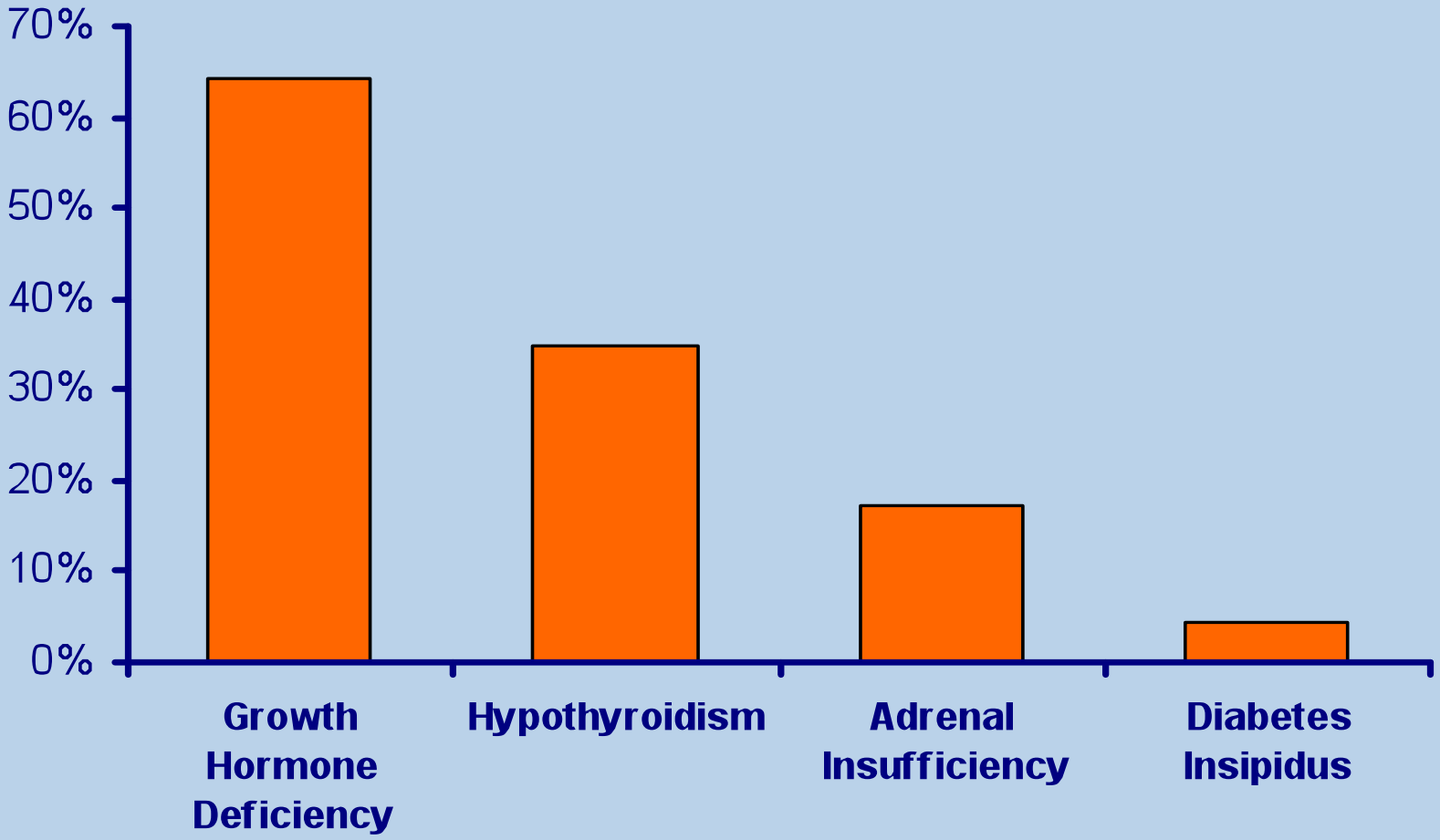
Signs of Hypothalamic Dysfunction

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

Hypopituitarism

- 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

Any endocrine dysfunction

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

Hypothyroidism

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

Newborn Thyroid Function

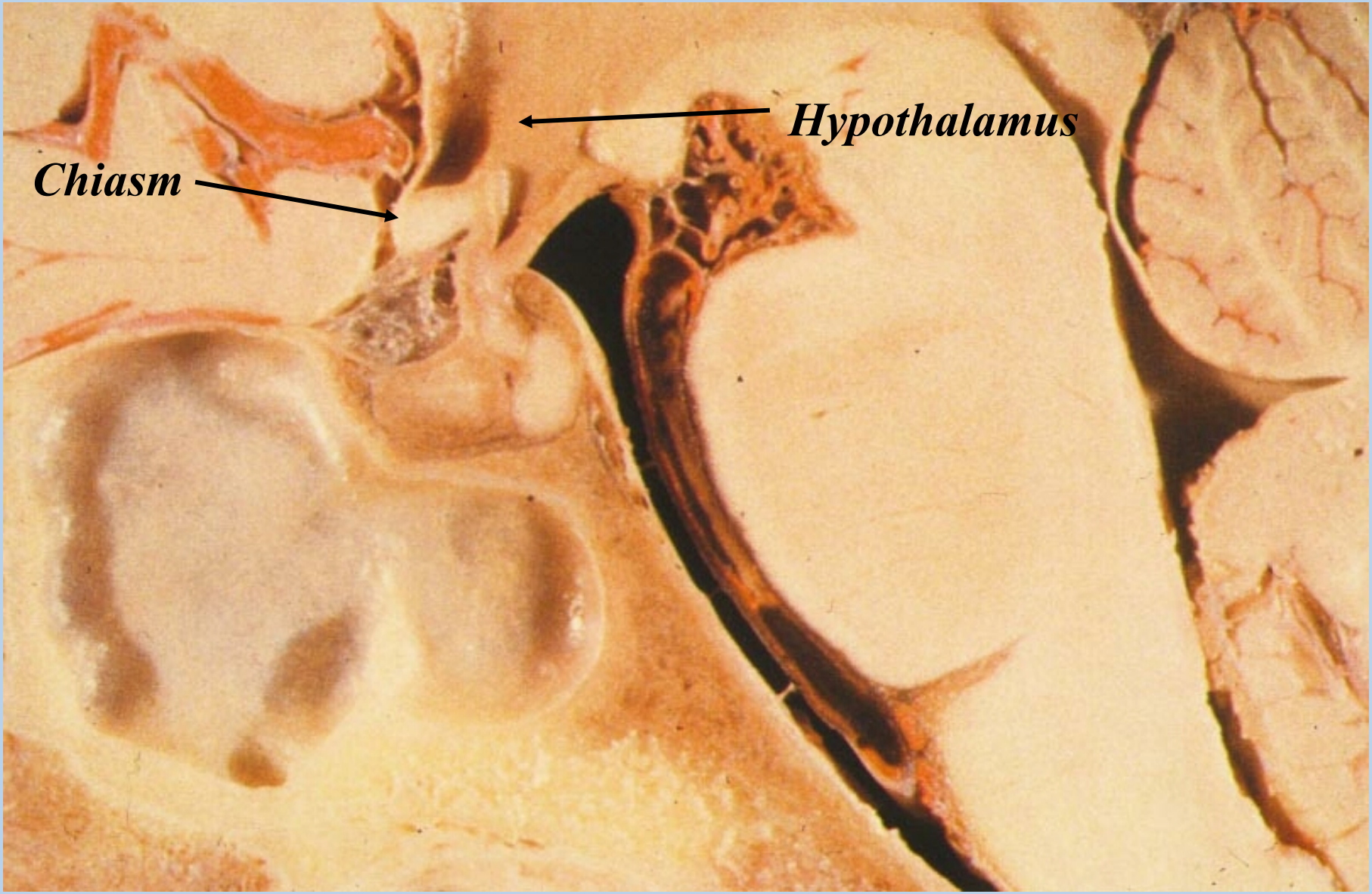
- Thyroid hormone essential for brain development in infants
- Newborn screening (NBS) for primary hypothyroidism (1/3000) mandatory in U.S.
- High (>25μIU) TSH reported by Calif. NBS
  - 94% sensitive for primary hypothyroidism
- Low TSH (associated with central hypothyroidism) not reported

Hypothyroidism & Vision in ONH

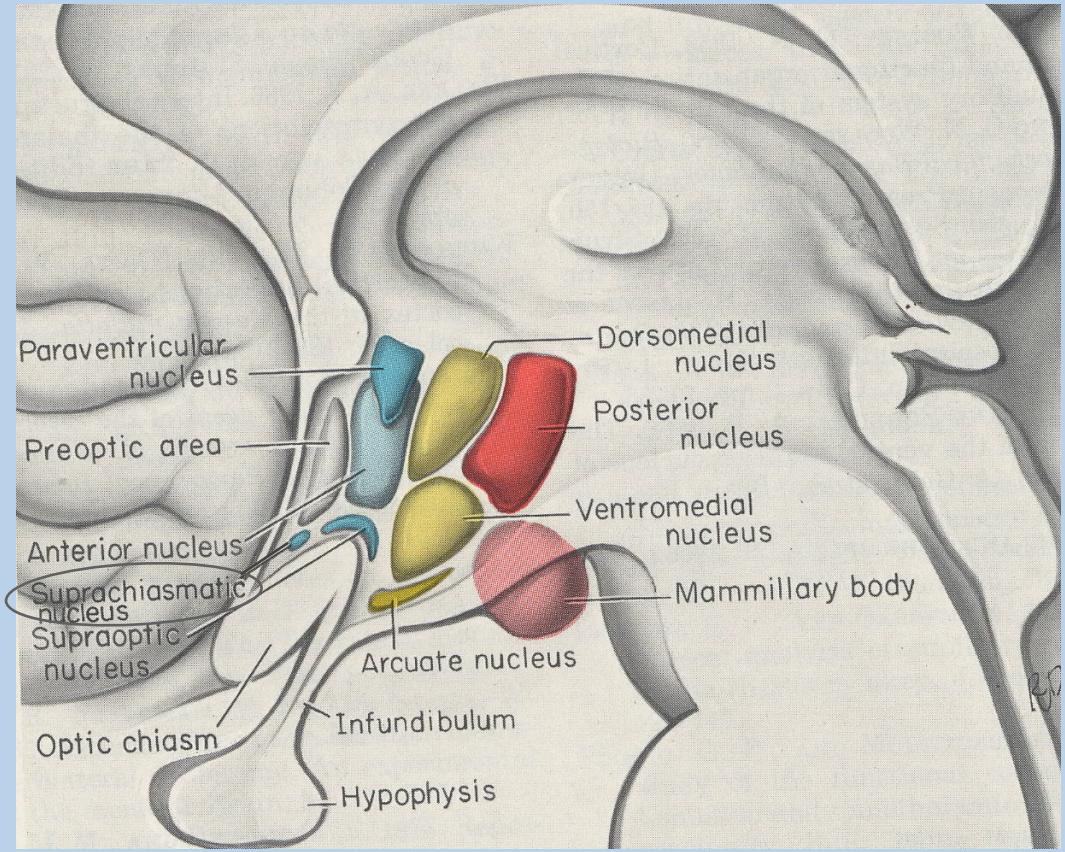
- Central hypothyroidism detected in ONH at mean age of 15 mos.
- Hypothyroidism is major risk factor for cognitive impairment in ONH
- Vision improves over 4-5 years in most children with ONH
- Thyroid hormone essential for optic nerve myelination in rodents

Laterality & Developmental Delay

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

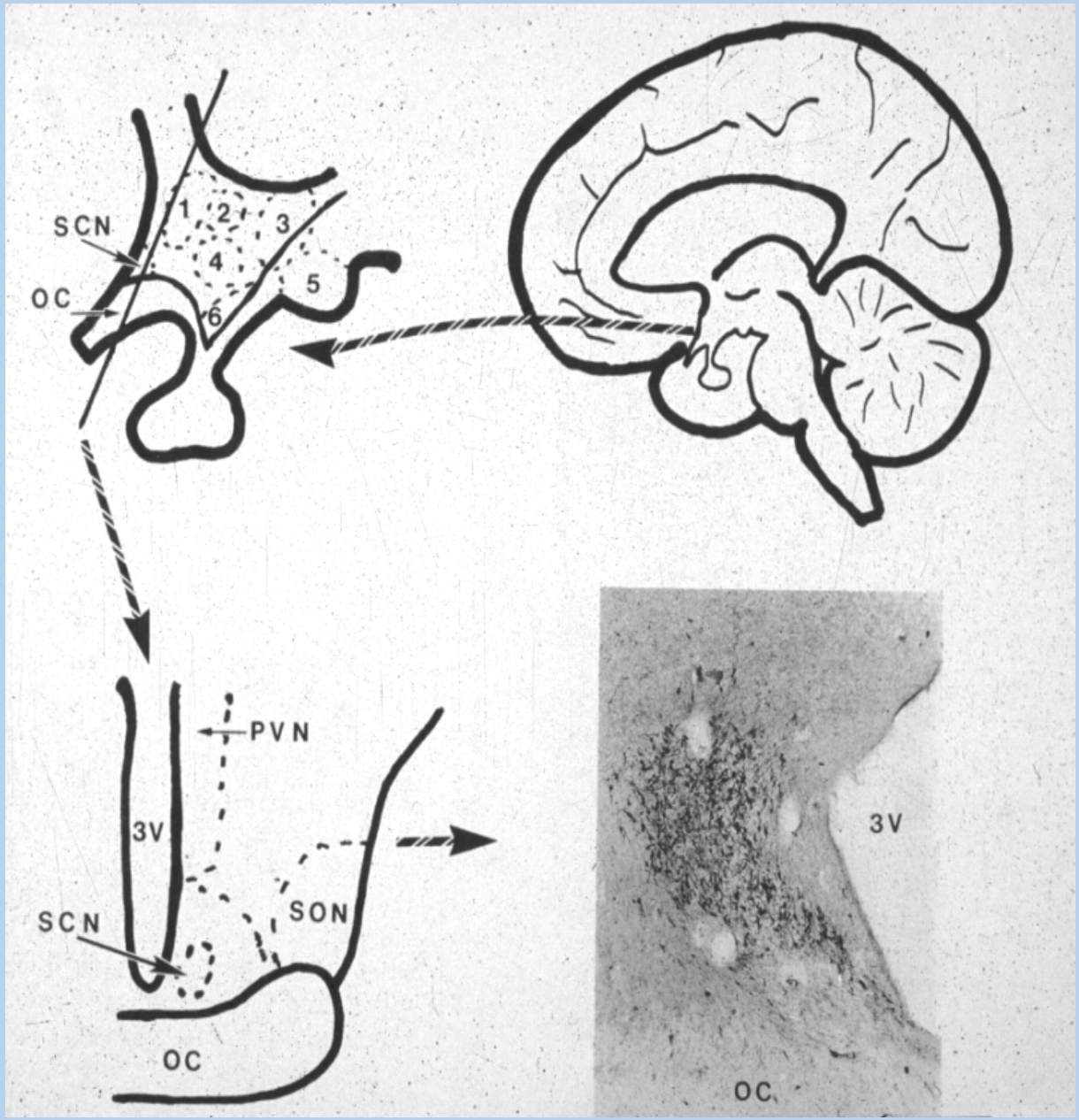

Hypothalamus
Chiasm

Hypothalamus & Sleep Regulation



<u>Suprachiasmatic Nucleus</u>:

- Located in hypothalamus
- Controls circadian rhythms


SCN
OC
1
2
3
4
5
6
PVN
3V
SCN
SON
OC
3V
OC

Circadian Rhythm

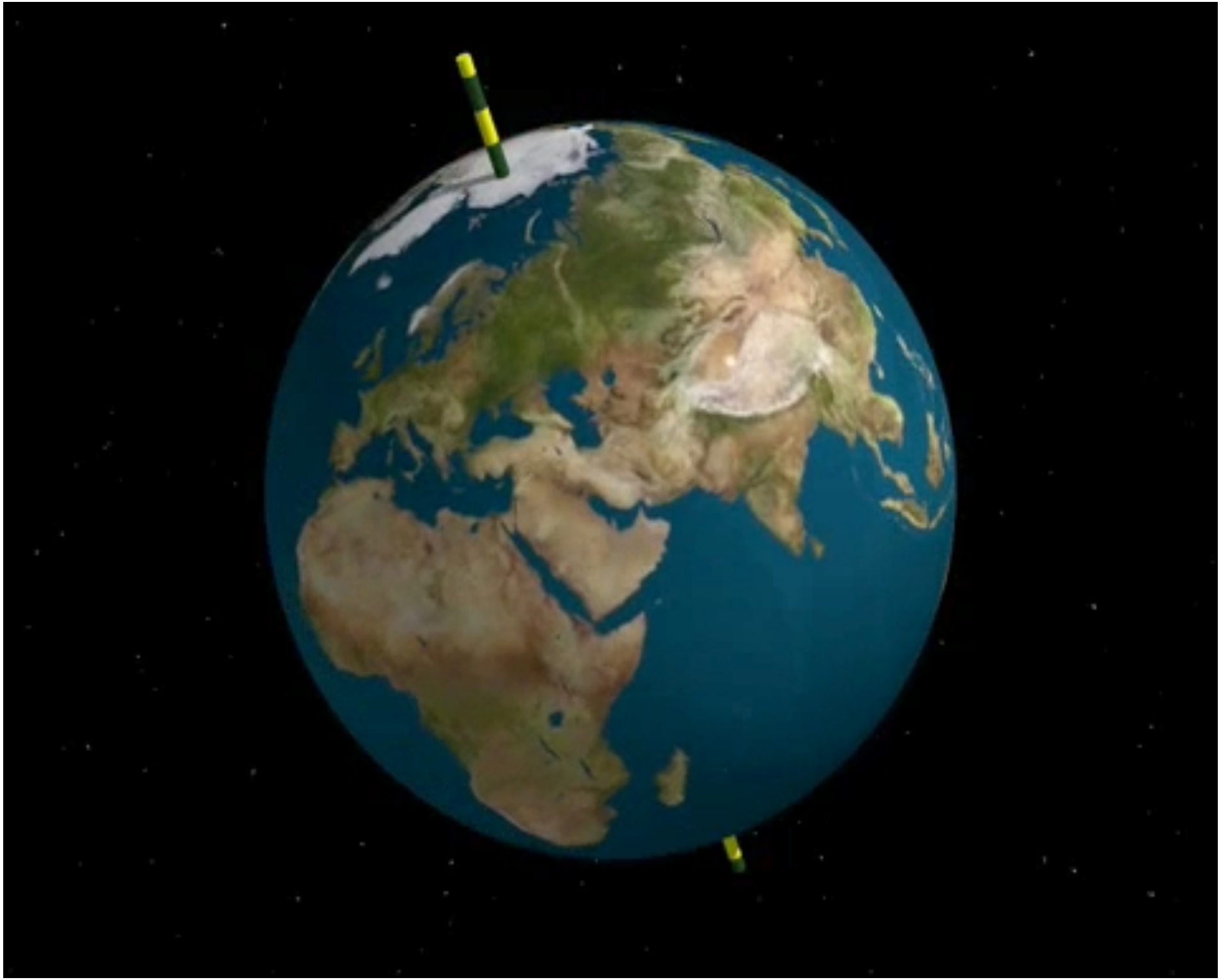
- Most cells of body have natural metabolic cycles.
- SCN neurons synchronize metabolic cycles of all cells approximately every 24 hrs.
- SCN suppresses release of melatonin from pineal gland.
- Melatonin suppresses brain and organ activity.

Circadian Rhythms

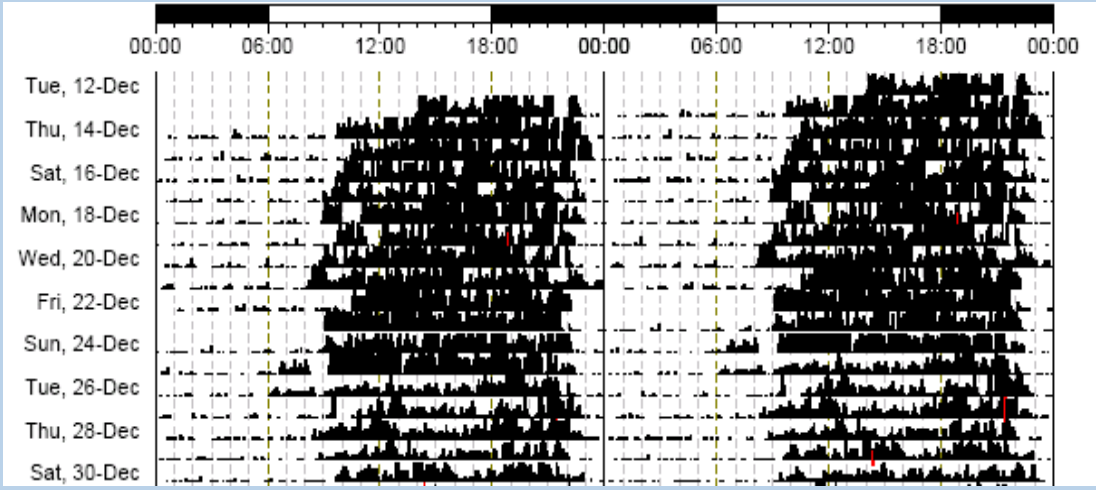
- Endogenously generated
- Period of about 24.2 hrs
- Examples:
  - Temperature rhythms
  - Hormone rhythms
  - Sleep-wake cycles
- Must be entrained to the solar cycle

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 Tmin causes later sleep next day.
  - Light exposure after Tmin causes earlier sleep next day.



Actigraphy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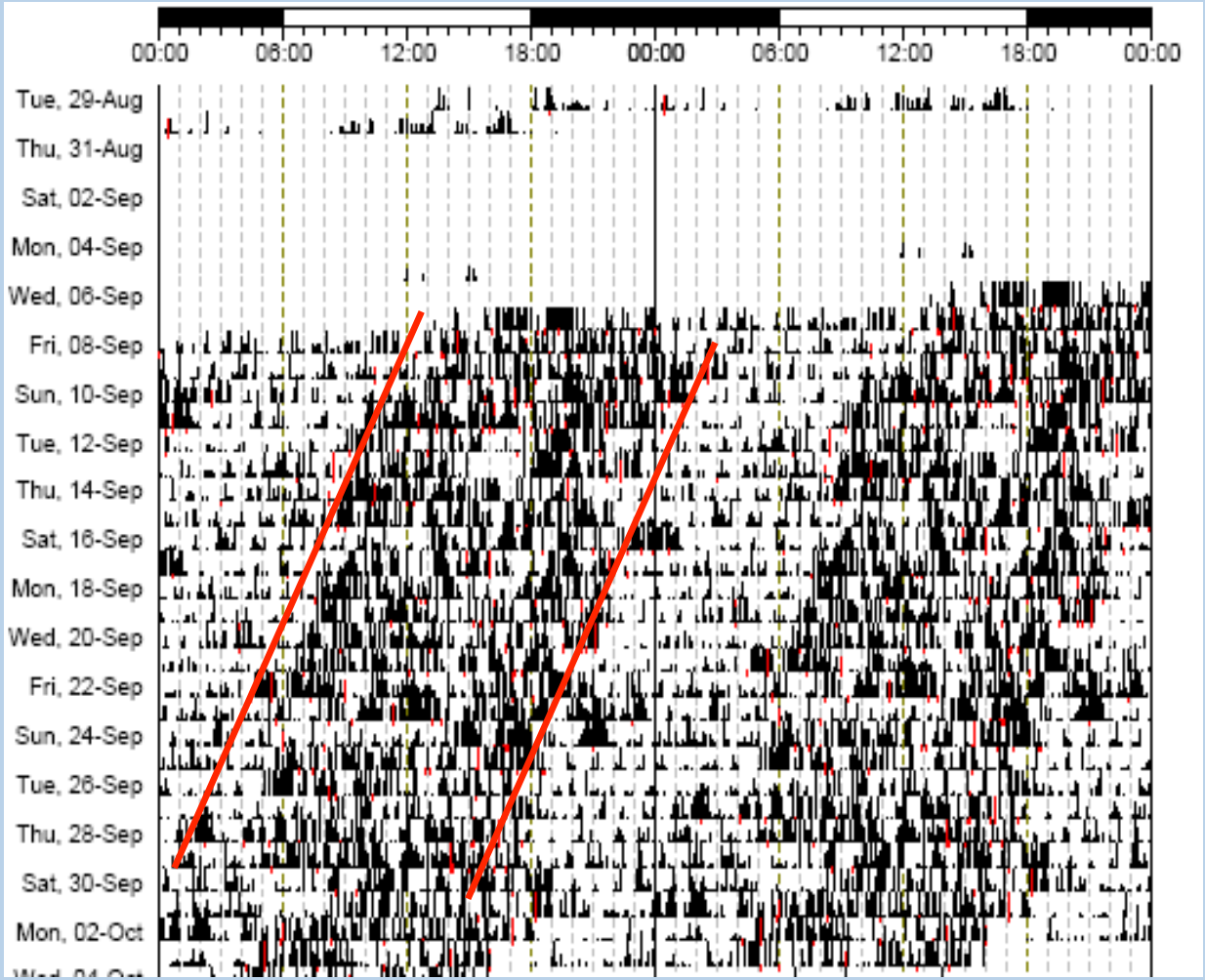
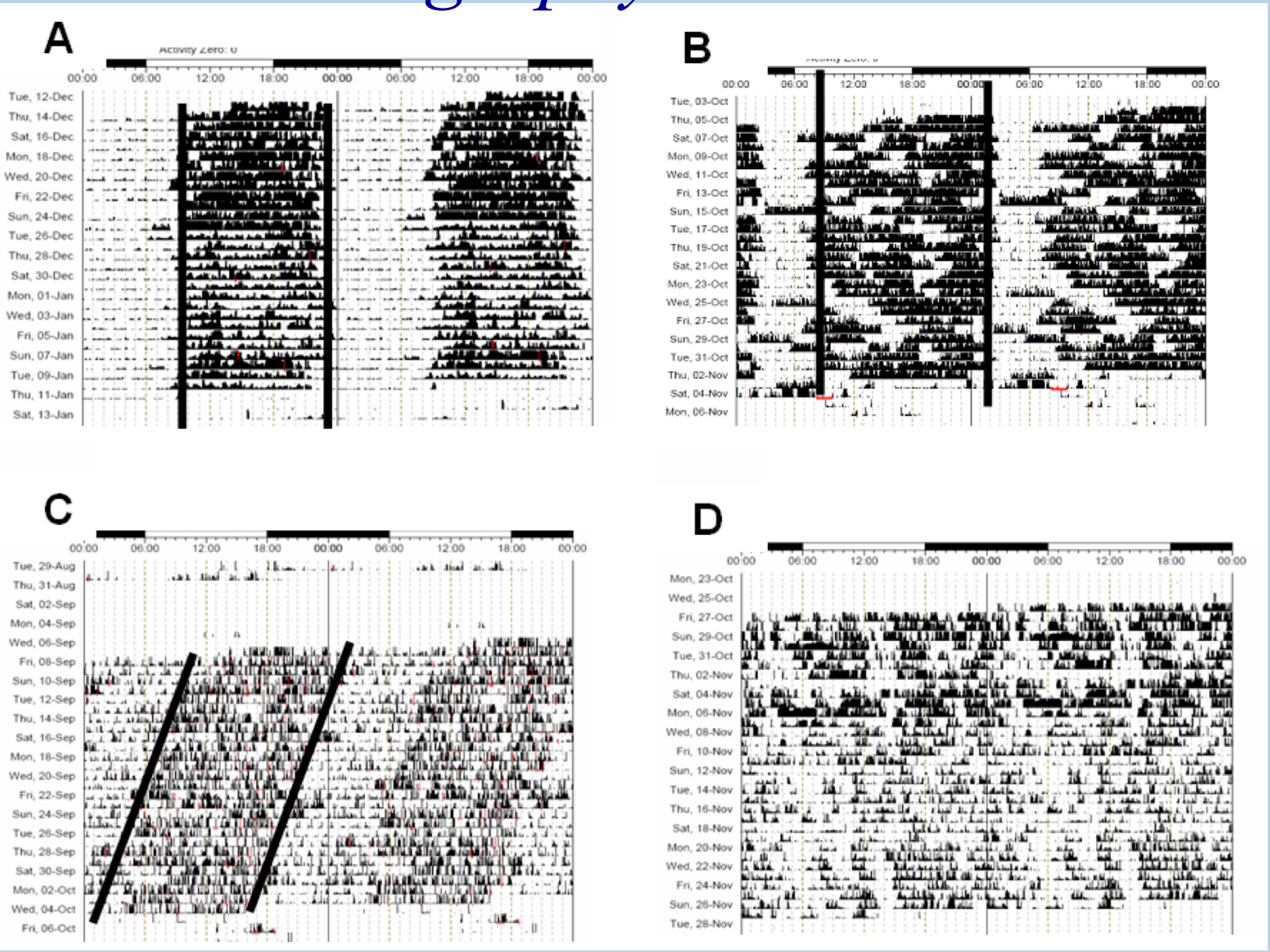
Free-running Sleep (no entrainment)



Actigraphy in ONH



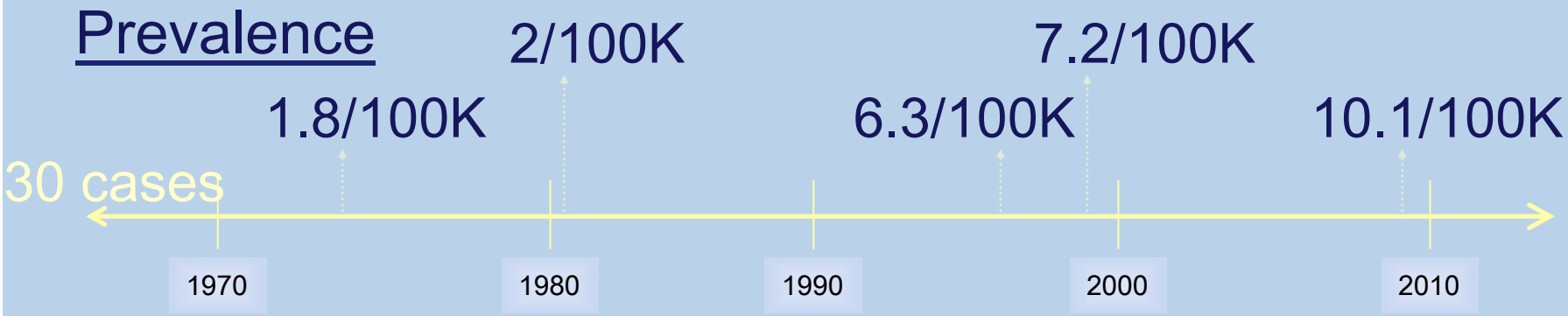
Clinical Associations with Sleep

	Normal rest-activity	Abnormal rest-activity	P-value
# Subjects	13	6	
Age (mos.)	44	40	0.45
Vision score	1.7	4.7	**.006**
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
≥3 hormone def.	7%	66%	**.03**
Dev. delay	15%	100%	**.04**

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 †

Scandinavia: 1999 *vs* 1980

↑ optic nerve hypoplasia

↓ other ocular disease

†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†
  - Disease events associated with factors of deprivation
    - Young maternal age, single, low education, unemployment

† Patel 2006

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 ± 6 years (*vs* 27.2 yrs)]
- Predominance of primiparous mothers

Table 3. Infant and Maternal Characteristics at Birth

Category (N*)	n	%	2000 Birth Data (%)	p-value
Mother's Age at Birth (n=196)				
< 20	58	30	12	
20-24	71	36	25	
25-29	41	21	27	<0.001
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

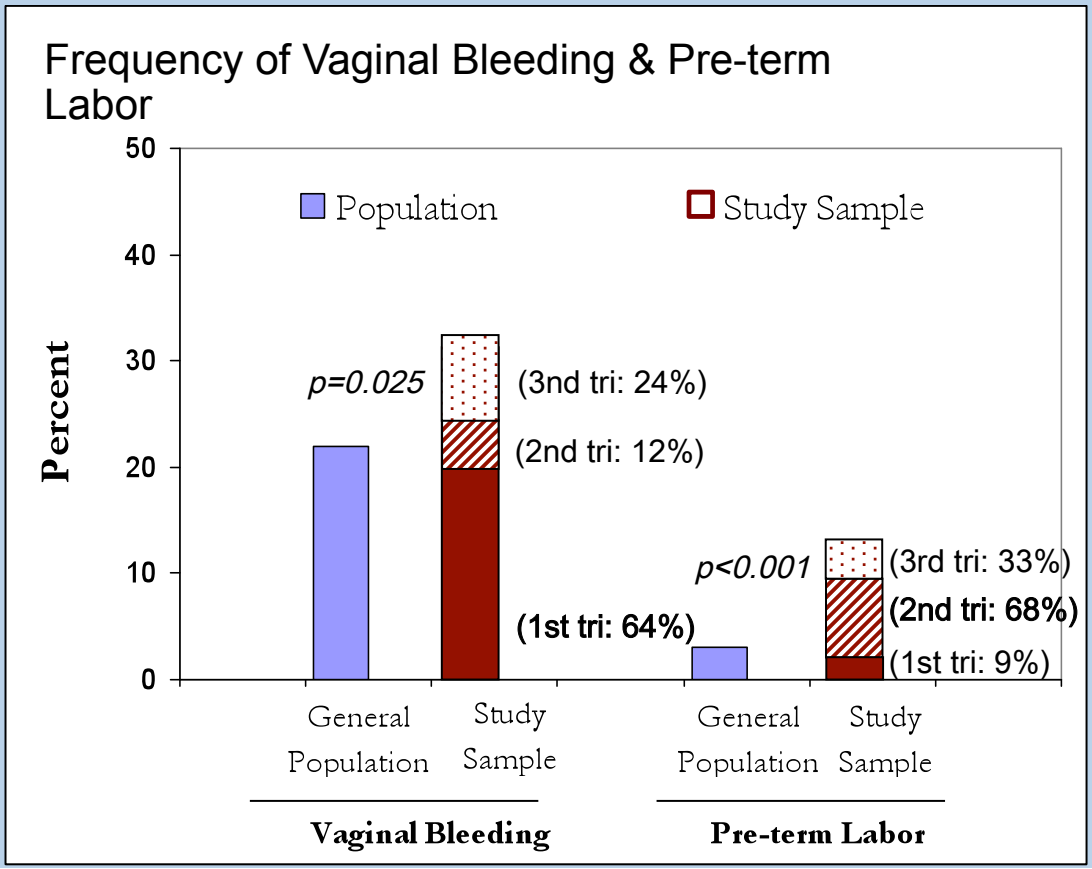
Refuted risk factors

- 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†

BMI Categories	% Low Wt Gain		p-value	Recommended Wt Gain† (lbs)	Average Wt Gain[a]
	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

† According to Institute of Medicine (IOM) (1990) guidelines.

[a] 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 1st or 2nd 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: 1st 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 1st trimester, and during the 2nd 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

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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 ☐

City or County ☐

State ☐

Block number example:
1826 Street Name
1800 is the block number

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

A. Zipcode ☐

OR

B. Block Number & Street Name ☐

City or County ☐

State ☐

Block number example:
1826 Street Name
1800 is the block number

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

A. Zipcode ☐

OR

B. Block Number & Street Name ☐

City or County ☐

State ☐

Block number example:
1826 Street Name
1800 is the block number

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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 affect 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

- www.onesmallvoicefoundation.org
- www.onhsurvey.org

Thank you