Timing is everything: Converging evidence for prediction of language delays from infancy to later childhood

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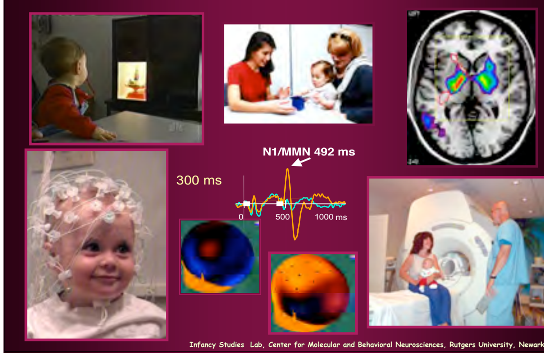

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EARLY LANGUAGE ACQUISITION

Most children easily and efficiently acquire language!

SPECIFIC LANGUAGE IMPAIRMENT

- However, a subset of children have a quite protracted and difficult time in acquiring language while other cognitive abilities appear to remain relatively intact. These children are said to have Specific Language Impairment (SLI) or developmental dysphasia.
- This classification is applied to children who present with a form of developmental language disorder that can not be attributed to a known cause such as hearing impairment, mental retardation, childhood schizophrenia, infantile autism, or frank neurological disorders.
- About 5% to 10% of all children beginning school are estimated to have such disorders (Robinson 1987, Tallal 2004; Tomblin 1996).

For REVIEW: Heim & Benasich, 2006, "Disorders of language." In D. Chicchetti and D. Cohen (Eds), *Developmental Psychopathology*, 2nd Edition, New York: John Wiley & Sons.

SPECIFIC LANGUAGE IMPAIRMENT

- Theories proposed to account for SLI range from arguments for the impairment of innate brain modules specialized for processing grammar (Gopnik & Crago,1991), to limitations in processing capacity or working memory (Gathercole & Baddeley, 1990; Schul, Stiles, Wulfeck & Townsend, 2004).
- SLI has traditionally been attributed to delays in the learning of semantic and syntactic rules critical to development of language (e.g. Clahsen, 1992; Rice &Wexler, 1996).

For REVIEW: Heim & Benasich, 2006, "Disorders of language." In D. Chicchetti and D. Cohen (Eds), *Developmental Psychopathology*, 2nd Edition, New York: John Wiley & Sons.

SPECIFIC LANGUAGE IMPAIRMENT

Another fundamental deficit implicated, and thought to be causal, in children with language or reading deficits is poor phonological processing (e.g. Bird, Bishop, & Freeman, 1995; Elliott, Hammer, & Scholl, 1989; Liberman, 1996; Scarborough, 1990; Wagner & Torgesen, 1987; Whitehurst & Fischel, 1994).

However, increasingly strong evidence suggests that differences in the basic auditory processing abilities of SLI children may also be related to their language deficits.

Many children with SLI go on to develop dyslexia supporting the view that developmental language disorders might share a common etiology (e.g. Bishop & Snowling, 2004)

Links Between Auditory Temporal Processing Abilities and Language-based Learning Disorders

Children with SLI hear normally and can sequence sounds, but are selectively impaired in their ability to separate successive rapid brief sounds of similar frequencies. Decoding of such stimuli are critical for mounting language.

Show excessive amounts of interference (auditory backward masking) when two auditory stimuli are presented in rapid succession (e.g.Wright et al., 1997; Wright, Bowen, Zecker, 2000).

Difficulties in processing brief, rapid successive auditory cues could impair or delay formation of distinct, phonological representations and so may play a causal role in SLI. Might also impede phonome to grapheme mapping critical to early reading. (Benasich, 2002; Benasich & Tallal, 2002; Benasich et al., 2006).

REVIEW: in Benasich Thomas, Choudhury, & Leppänen, Dev. Psychobiology, 2002, 40.

Links Between Auditory Temporal Processing Abilities and Language-based Learning Disorders

Neurons specialized for processing rapid transient stimuli (magnocellular neurons) in both visual and auditory thalamic regions have been implicated in the temporal processing deficits seen in SLI and dyslexic subjects (e.g. Eden et al. 1995, Galaburda et al. 1994; Herman et al. 1995; Livingstone et al. 1991; Witton et al., 1998).

Imaging studies show atypical patterns of cerebral lateralization in SLI & dyslexic individuals as compared to controls. Specifically, a lack of normal left-greater-than-right pattern is seen in the planum temporale as well as in parietal and frontal regions (e.g. Jernigan et al. 1991; Larson et al. 1990; Leonard et al. 1993; Neville et al. 1993; Plante et al. 1991, 1996)

REVIEW: in Benasich, Thomas, Choudhury, & Leppänen, Dev. Psychobiology, 2002, 40.

WHY LOOK IN EARLY INFANCY?

EVIDENCE FOR EARLY ORIGINS OF SPECIFIC LANGUAGE IMPAIRMENT

- Early Auditory and Speech Competence
- Heritability Evidence
- Neuropathological studies revealing brain abnormalities (e.g., ectopias, microgyric lesions, and asymmetries)

QUESTION

What role does efficient processing of brief, rapidly-presented, successive auditory stimuli in early infancy play in early language acquisition?

ORIGINAL SERIES OF PROSPECTIVE LONGITUDINAL STUDIES

GENERAL TASKS

Experimental and Standardized Tasks of:
- Information Processing,
- Language and Cognition,
- Social interaction and Play

Electrophysiology using EEG/ERPs

Brain mapping with structural MRI's

BEHAVIORAL PERCEPTUAL-COGNITIVE BATTERY

- Visual Habituation & Recognition Memory Tasks
- Auditory-Visual Habituation & Recognition Memory Tasks
- Rapid Auditory Processing Tasks
  - 2 Alternative Forced-Choice Task
  - Oddball Operantly Conditioned Head-turn Task
- Cognitive and Language Assessment

ALL INFANTS ARE OR WILL BE TESTED LONGITUDINALLY AT:
3, 6, 9, 12, 16, 24, 36, 48, 60, 72, and 84 months

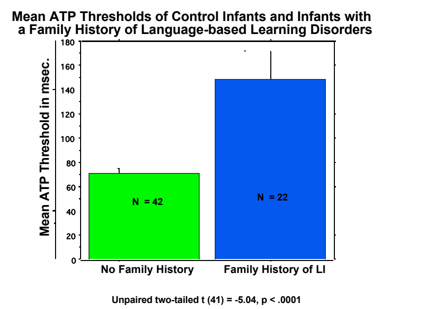
Two Alternative Forced-Choice Procedure

Infants are operantly conditioned to discriminate between two auditory tone sequences and associate each 2 tone auditory stimulus with a directional response (right vs. left).

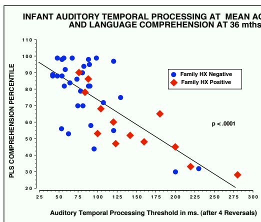
They must anticipate which of two toys will be illuminated and set in motion by making a head-turn to the correct place.

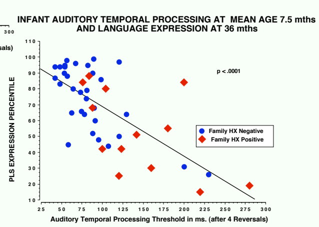
STIMULI: Two 75 ms Complex Tone Pairs with fundamental frequencies of 100 and 300 Hz.

Discrimination is to same vs. different tone pairs with varying ISIs (e.g. 100-100 Hz vs. 100-300 Hz).



Benasich & Tallal (1996). Infant Behavior and Development, 19, 339-357.





PROCESSING THRESHOLDS IN INFANCY ARE RELATED TO LATER LANGUAGE AT ALL SUBSEQUENT AGES

Benasich & Tallal 2002, Behavioral Brain Research, 136 (1), 31-49; Benasich, et al. 2002, Developmental Psychobiology, 40, 278-292.

HIERARCHICAL STEPWISE REGRESSIONS

RESULTS:

RAP threshold accounted for largest amount of variance in language scores and verbal subsets of Stanford-Binet at 36 months. (29% to 52%)

Gender accounted for second largest amount of variance.

Analyses with Quantitative and Abstract Reasoning Subscales of S-B were not significant.

Benasich, A.A. & Tallal, P. (2002). *Behavioral Brain Research*, *136* (1), 31-49

DISCRIMINANT FUNCTION ANALYSES

Outcomes on the Verbal Reasoning Subscales of the Stanford-Binet at 36 months were examined:

V/R Comprehension Test
V/R Vocabulary Test

Subscale mean=50, SD=8
Defined “impaired” as 1 SD below the mean

Benasich, A.A. & Tallal, P. (2002). *Behavioral Brain Research, 136* (1), 31-49

DISCRIMINANT FUNCTION ANALYSES

Classification accuracy to impaired vs. nonimpaired groups using SB V/R Subscales at 36 mths (N=33):

V/R Vocabulary Test: 93.9% (p < .001)
V/R Comprehension Test: 90.9% (p < .001)

A logistic procedure identified RAP Threshold as the determining variable.

Chi Square for RAP In/Removed :
Vocabulary Test: 14.7 (p> .0001) but 1.2 (p> .279)
Comprehension Test: 7.2 (p> .01) but 4.5 (p> .03)

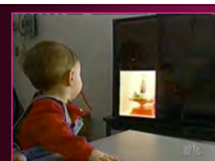
Benasich, A.A. & Tallal, P. (2002). *Behavioral Brain Research, 136* (1), 31-49

DISCRIMINANT FUNCTION ANALYSES

Using information about processing abilities at infancy, we can quite accurately identify children who will be impaired at age 3.

TRUE FOR BOTH FH+ AND FH- CONTROLS

Benasich & Tallal, 2002; Benasich et al., 2002 ; Choudhury & Benasich, 200



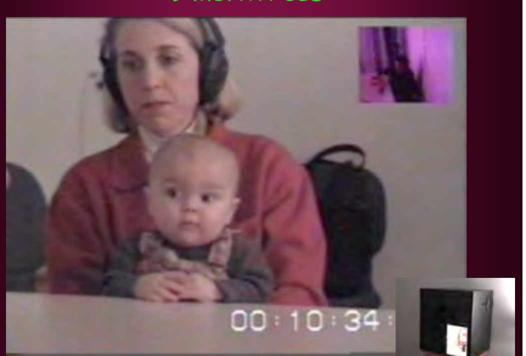
REPLICATION Using Go/No-Go Head-turn Procedure

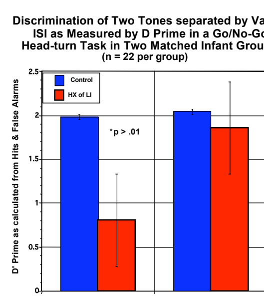
Infants are operantly conditioned to make a head-turn to the reinforcer following a target tone sequence embedded within a standard repeating sequence.

Discrimination is to same vs. different (e.g. 100-100, 100-100, 100-300, 100-100)

STIMULI: 75 ms Complex Tone Pairs
e.g. 100Hz-100Hz & 100Hz-300Hz
Test blocks with within-pair ISIs of 10, 70 ms, 300 & 500 ms

CONDITIONED HEAD-TURN/ AUDITORY ODDBALL: 9 MONTH OLD

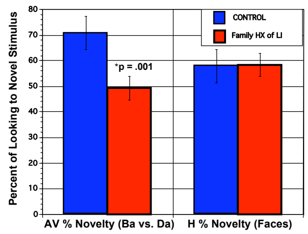




REPLICATION OF DIFFERENCES AS A FUNCTION OF FAMILY HISTORY.
50% ARE IMPAIRED

Benasich & Leevers (2002). Progress in Infancy Research, Vol. 3. (pp. 245-288).

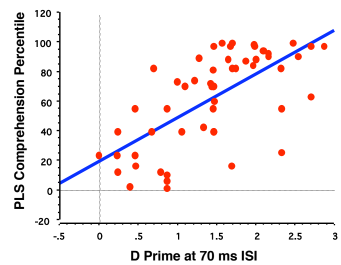
Discrimination of Consonant-Vowel Syllables (Ba vs Da) as compared to Face Discrimination in Infants with a Family History of LI (n = 22) and Matched Controls



INFANTS WITH A POSITIVE FAMILY HISTORY FOR LI ARE IMPAIRED ON BOTH SPEECH AND NONSPEECH RAPID SOUND PAIRS

Benasich & Leevers (2002). Progress in Infancy Research, Vol. 3. (pp. 245-288).

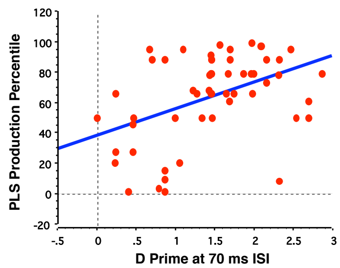
Auditory Temporal Processing at 6 Months & Language Comprehension at 24 Months



PLS COMP%.24 = 19.496 + 29.508 * DP70; R^2 = .445, p < .0001

THESE EARLY DIFFERENCES ARE ALSO RELATED TO LATER LANGUAGE OUTCOME IN BOTH CONTROL INFANTS AND FAMILY HISTORY INFANTS

Auditory Temporal Processing at 6 Months & Language Production at 24 Months

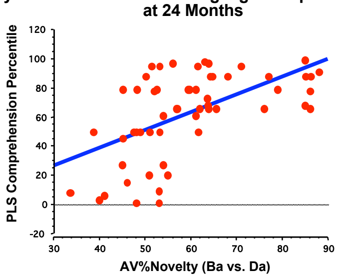


PLS CMP %.24 = 38.347 + 17.461 * DP70; R^2 = .189, p = .001

Benasich et al. (2002). Developmental Psychobiology, 40, 278-292.

AUDITORY/VISUAL HABITUATION: 6 MONTH OLD

Discrimination of Consonant-Vowel Syllables at 6 Months & Language Comprehension at 24 Months



PLS EXP%.24 = -10.181 + 1.222 * AVH%N; R^2 = .323, p< .0001

EARLY DIFFERENCES IN CV DISCRIMINATION ARE ALSO RELATED TO LATER LANGUAGE OUTCOME

Benasich et al., 2001

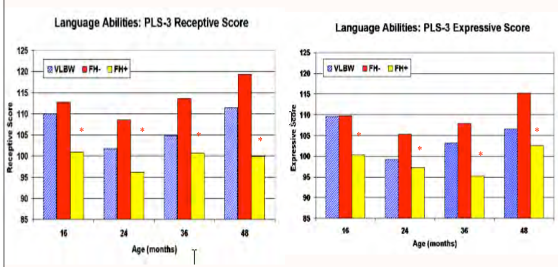
Cognitive abilities 36 – 60 months Stanford-Binet Intelligence Scale

Variable	Age	VLBW Mean	VLBW SD	FH- Mean	FH- SD	FH+ Mean	FH+ SD	F	p
Verbal Reasoning	36-m	103.78	11.7	112.73	12.5	104.95	13.2		
	48-m	107.26	10.7	116.69	9.2	109.50	13.9		
	60-m	104.70	8.4	113.38	7.0	111.36	13.0	5.44	0.006*
Abstract/Visual Reasoning	36-m	96.43	12.2	107.19	8.5	103.27	11.0		
	48-m	96.43	12.2	105.85	12.7	99.68	9.4		
	60-m	93.22	13.2	106.46	12.9	101.05	14.7	7.56	0.001*
Quantitative Reasoning	36-m	98.36	10.2	104.70	11.4	105.11	13.2		
	48-m	100.64	11.0	108.35	11.2	101.06	17.9		
	60-m	97.64	10.7	102.22	9.7	105.78	12.4	5.46	0.007*
Short Term Memory	36-m	106.87	10.4	112.23	9.3	107.95	11.9		
	48-m	99.83	13.94	107.92	10.0	101.33	15.6		
	60-m	98.09	9.4	105.00	13.5	99.24	14.7	3.20	0.047*
Composite Score (IQ)	36-m	101.39	10.5	111.04	8.7	105.59	13.3		
	48-m	101.26	10.2	111.42	8.4	104.27	12.4		
	60-m	98.17	9.4	110.15	9.8	105.18	13.0	7.27	0.001*

* $p < 0.05$

Ortiz-Mantilla, Choudhury, Leevers & Benasich, In Press: Developmental Psychobiology

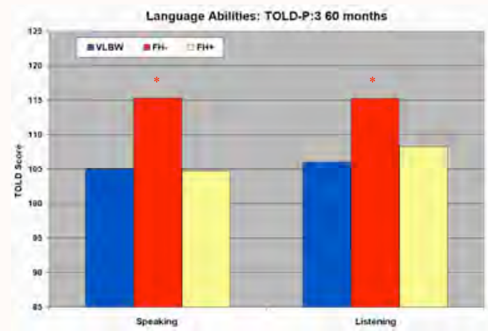
Language abilities 16 – 48 months



* p < 0.05

Ortiz-Mantilla, Choudhury, Leevers & Benasich, In Press: Developmental Psychobiology

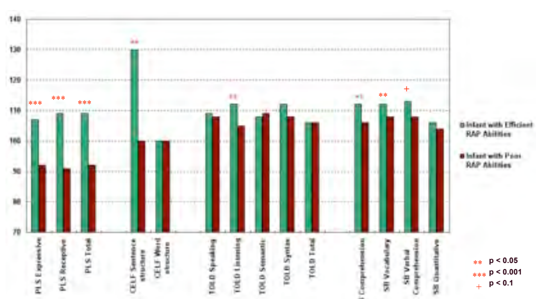
Language abilities 60 months



* p < 0.05

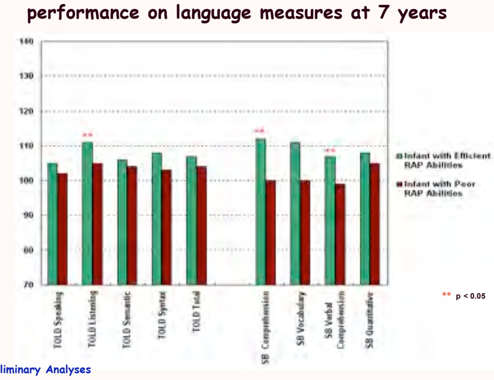
Ortiz-Mantilla et al. In Press: Developmental Psychobiology

Infant RAP abilities (6-9 months) and performance on language measures at 5 years



Preliminary Analyses

Infant RAP abilities (6-9 months) and performance on language measures at 7 years



Preliminary Analyses

SUMMARY: INFANT BEHAVIORAL STUDIES

- Our data lend support to the notion that the ability to perform fine acoustic discriminations (within speech or non-speech) in early infancy is critically important to later language development.
- Temporal processing deficits have been demonstrated before spoken language emerges and is a reliable predictor of later language.

SUMMARY: INFANT BEHAVIORAL STUDIES

IMPORTANTLY:

- We have also shown that our infant measures predict language and verbally -related outcomes in normally developing control populations through age three.
- Preliminary evidence suggests we can predict to poor language attainment through age 7 years.

QUESTIONS REGARDING BRAIN & BEHAVIOR

How might we address issues relating to identification of neural substrates involved in processing of rapidly changing auditory cues as well as specific linguistic stimuli across development ?

Behavioral and electrophysiological data can be linked in order to more fully address the original questions and identify neural substrates.

EEG/ERPs and Structural Analyses

ERP setup at Infant Studies Laboratory, CMBN, Rutgers University

ERP Setup at Infant Studies Laboratory, CMBN, Rutgers University

64- and 128-Channel Geodesic sensor nets (Ag/AgCl electrodes on soft sponges) allow us to:

- measure continuous EEG (with sampling rate up to 500 Hz) from which event-related brain activity can be extracted
- apply evenly spaced sensors across different scalp areas painlessly and quickly – useful for infants and children

Analysis techniques include:

- ERP averaging and 2D/ 3D topographical electric field maps and animations
- brain electrical source analysis for locating generator dipoles
- Mapping function to structure using structural MRIs and Brain Voyager software.

ERP Procedure for Tones

Stimuli
2 complex tones were presented in tone pairs:
•low-low 100-100 Hz
•low-high 100-300 Hz
•70 ms duration for each tone
•Oddball paradigm with 15% Deviant and 85% Standard.

Predicting From Event-Related Potentials to Behavior: Auditory ERPs to 70 and 300 ms ISI tone pairs

PARTICIPANTS:
15 (FH+) full-term infants born into families with a history of SLI
30 (FH-) full-term infants with no family history of SLI

Assessed at 6, 12, 16, 24 and 36 months of age using a battery of assessments:
EEG/ERPs, habituation and recognition memory, operantly conditioned head-turn, standardized cognitive and language measures, temperament, mother-infant interaction

Deviant, 100-300 Hz, 15 %
Standard, 100-100 Hz, 85 %

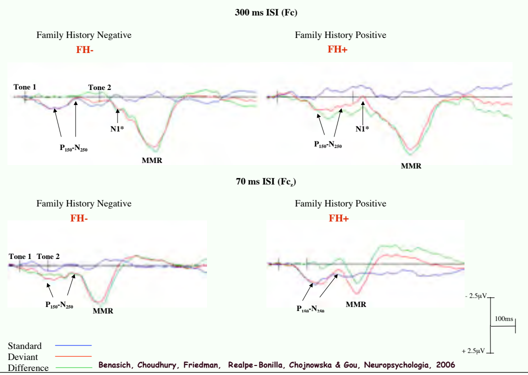
Benasich et al., 2006

ERP TO AUDITORY ODDBALL: 9 & 12 MONTHS

ISI = 300 ms ⇓

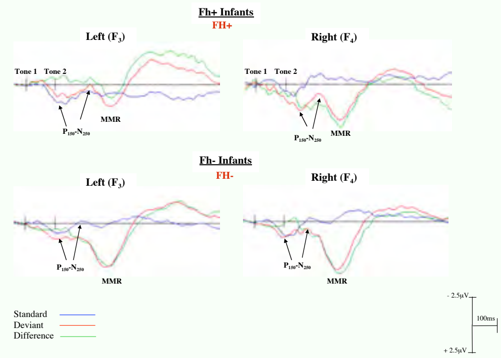
ISI = 70 ms ⇑

ERP waveforms to 300- and 70-ms ISI conditions for Fc_z (electrode 4) in FH- and FH+ infants



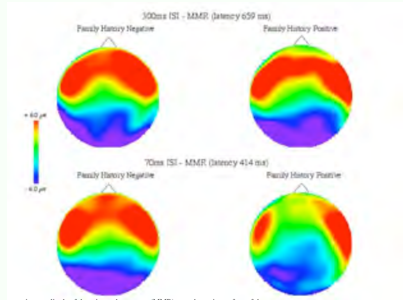
Benasich, Choudhury, Friedman, Realpe-Bonilla, Chojnowska & Gou, Neuropsychologia, 2006

ERP responses to 70 ms ISI stimuli in Fh+ and Fh- infants for F_3 (left 13) and F_4 (right 62) frontal channels



Benasich, Choudhury, Friedman, Realpe-Bonilla, Chojnowska & Gou, Neuropsychologia, 2006

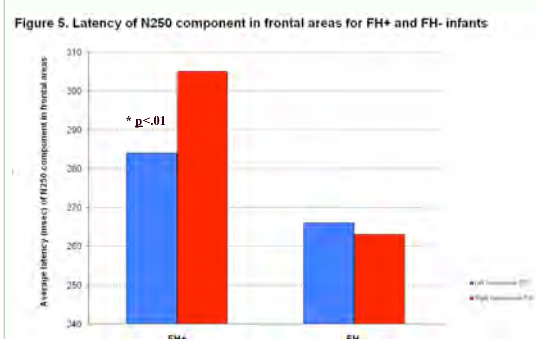
Topographic Maps of the MMR for 300 ms ISI and 70 ms ISI for FH+ and FH- Infants



. Topographic maps representing amplitude of the mismatch response (MMR) over the entire surface of the head for 300 ms ISI (top) and 70 ms ISI (bottom) are shown at peak MMR latency (659ms and 414 ms, respectively) for FH+ and FH- infants. Anterior to posterior represented top to bottom (nose at top). There are no significant group differences in the 300 ms ISI, but for the 70 ms ISI condition the FH+ infants show reduced positivity (MMR) at frontal, frontocentral and central channels as compared to the FH- infants. Additionally, FH+ infants demonstrated a significantly smaller MMR (reduced positivity) in the left hemisphere as compared to FH- infants. There was no significant group by hemisphere interaction for the right hemisphere.

Benasich et al., 2006

Averaged latency of the N_{250} ERP waveforms by hemisphere to the 70 ms ISI stimuli



*Latency by Group

Benasich, Choudhury, Friedman, Realpe-Bonilla, Chojnowska & Gou, Neuropsychologia, 2006

Summary of results of 6 month Auditory ERPs

FH + Infants as compared with FH- Infants

- At 6 months, well-defined differences were seen between groups in the amplitude of the mismatch response (MMR) as well as the latency of the N_{250} component in the 70ms ISI condition, but not the 300ms ISI condition.
- FH+ infants showed smaller MMRs and delayed onset of the N_{250} component as compared to infants without familial risk.
- Hemispheric pattern of response differed between groups only in the 70ms ISI condition.
- FH+ infants showed lower peak amplitudes in fronto-central areas of the left hemisphere as compared to the right, whereas the FH- controls showed no laterality differences .

Correlations between 6-month latency of response to 70ms ISI stimuli (N_{250}) and 24-month Expressive and Receptive Language Abilities for FH+ and FH- Infants (n=35)

	Left Hemisphere		*Right Hemisphere*	
	Expression	Comprehension	Expression	Comprehension
Brain Regions				
Frontal	-.50*	-.40*	-.40*	-.31*
Fronto-central	-.36*	-.35*	-.41*	-.40*
Central	-.47*	-.44*	-.02	-.05
Temporal	-.03	-.01	-.09	-.05
Parietal	.22	-.03	.16	-.05
Occipital	.44*	.28*	.48*	.31*

*p<0.05

Benasich, Choudhury et al. *Neuropsychologia*, 44, 2006, 396-411.

Summary of results of 6-month Auditory ERPs Language and 24-month Behavior

FH + Infants as compared with FH- Infants

- Group differences in brain activation to non-speech stimuli were significantly associated with differences in linguistic performance at 24 months-of-age.
- Both language comprehension and expression were correlated with the latency of the N_{250} component in the 70ms ISI condition.
- No associations were found between the group differences in amplitude of the MMR at 6-months and performance on standardized tests at 24 months.

Summary of results of Power Band Analyses of Resting EEGs

Differing patterns suggest delayed maturation of frontal areas or differing recruitment of brain areas.

Analyses of relations between individual power density function and behavioral performance show associations with concurrent receptive and expressive language and cognitive skills.

Power was also associated with attention measures; children who were observed as having better inhibitory control and more mature attention shifting abilities had higher power.

Gamma power was not associated with fine motor abilities, maternal behavior, parental SES or maternal education.

No correlations were significant for mean power from 5 to 30 Hz.

ANY ANSWERS?

1. Can the study of processing abilities in early infancy resolve the longstanding controversy as to the etiology and pattern of deficits seen in children with SLI?

YES-- although much research remains to be done, it is clear that we can identify those infants, who manifest less efficient processing of brief, rapidly presented auditory cues.

Further study of the type and degree of deficit in infancy may give us the ability to identify different mechanisms of impairment and connections to later etiology.

ANY ANSWERS?

2. Do rapid auditory processing deficits simply co-occur with the difficulties in phonological and syntactic decoding seen in children with SLI or do they precede and predict language impairments?

It appears that RAP deficits can be shown preverbally, well before the age at which phonological deficits would arise. Although causality has not yet been established, these deficits precede AND predict language delays. Need training studies!

ANY ANSWERS?

3. Could it be that the efficient processing of basic acoustic properties early in life is important to subsequent language and cognitive competence?

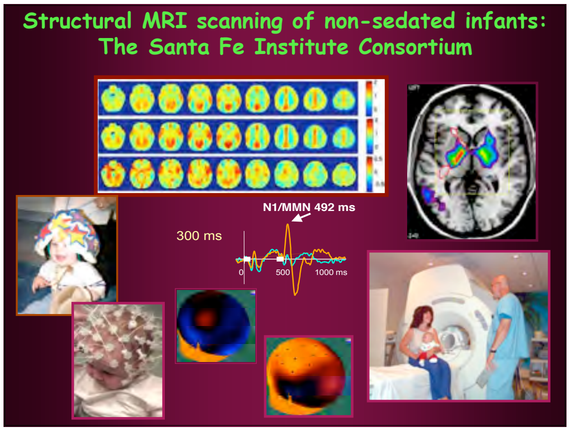
Efficient processing of basic acoustic properties early in life appears to be critically important to subsequent language for all children and almost certainly goes awry in a subset of infants who later present with language impairments.

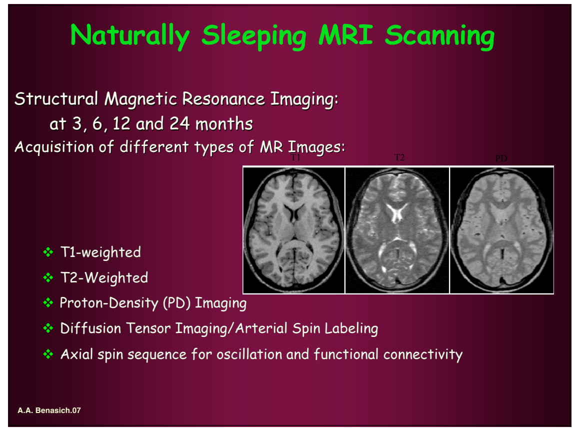
CONCLUSIONS

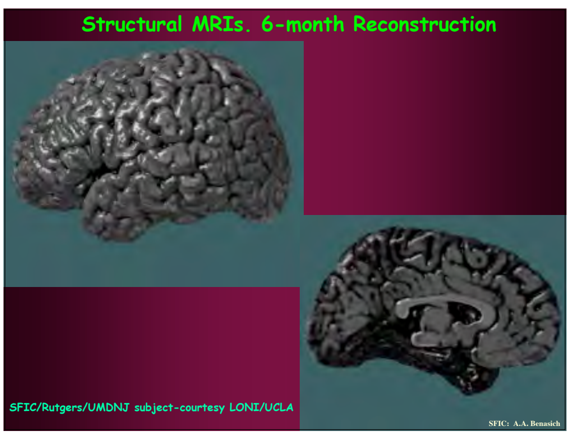
Our converging data lend support to the notion that the ability to perform fine acoustic discriminations (within speech or non-speech) in early infancy is critically important to later language development.

Further examination of fine-grained temporal dynamics is critical to understanding the brain and behavior interface underlying LI.

Infants may gain from early intervention based on selective screening, preventing their early impairments from exerting negative cascading effects on later language, academic, and social skills.


Structural MRI scanning of non-sedated infants:
The Santa Fe Institute Consortium
N1/MMN 492 ms
300 ms
0
500
1000 ms


Naturally Sleeping MRI Scanning
Structural Magnetic Resonance Imaging:
at 3, 6, 12 and 24 months
Acquisition of different types of MR Images:
T1
T2
PD
T1-weighted
T2-Weighted
Proton-Density (PD) Imaging
Diffusion Tensor Imaging/Arterial Spin Labeling
Axial spin sequence for oscillation and functional connectivity
A.A. Benasich.07


Structural MRIs. 6-month Reconstruction
SFIC/Rutgers/UMDNJ subject-courtesy LONI/UCLA
SFIC: A.A. Benasich