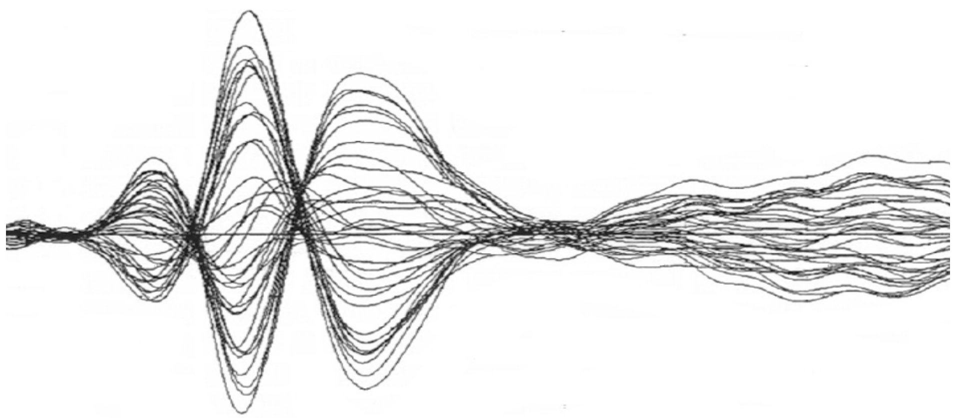
University of California · Irvine

MEG Investigations of Neural Synchrony in Auditory Language Cortex in Children with Autistic Disorder, their Siblings, and Typically Developing Controls



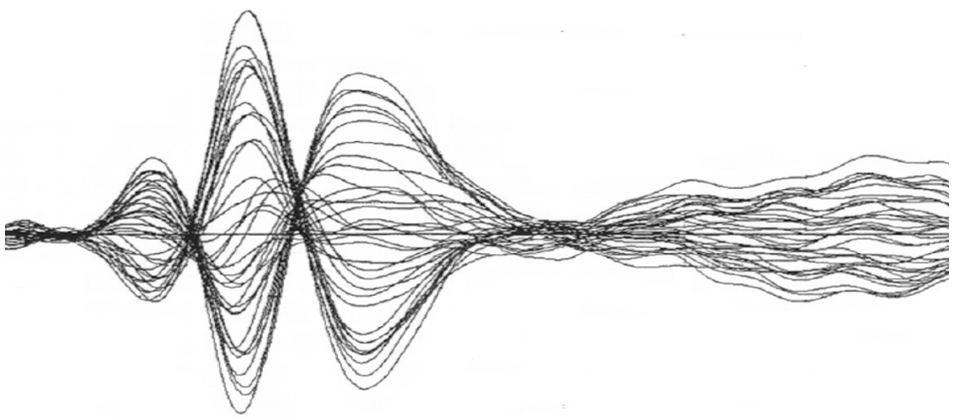
Nicole M. Gage, PhD

Cognitive Neuroscience of Language Lab
Department of Cognitive Sciences
University of California, Irvine

center for COGNITIVE NEURO SCIENCE
the University of California, Irvine

UNIVERSITY of CALIFORNIA · IRVINE

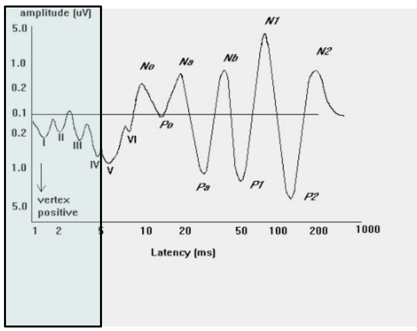
It's about time …



Nicole M. Gage, PhD
Cognitive Neuroscience of Language Lab
Department of Cognitive Sciences
University of California, Irvine

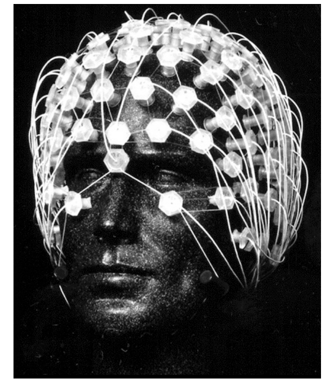
center for COGNITIVE NEURO SCIENCE
the University of California, Irvine

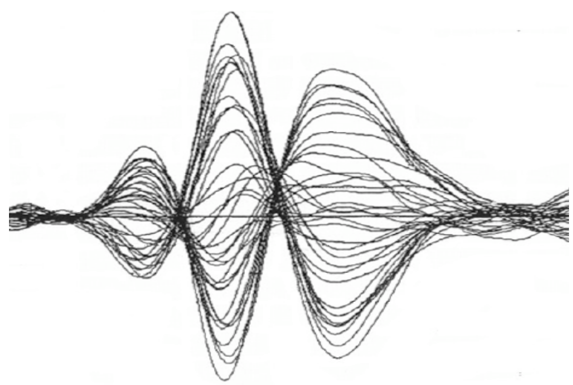
Multidisciplinary Investigations of the Auditory System



ABR and Audiometric investigations of the ascending and descending auditory pathways

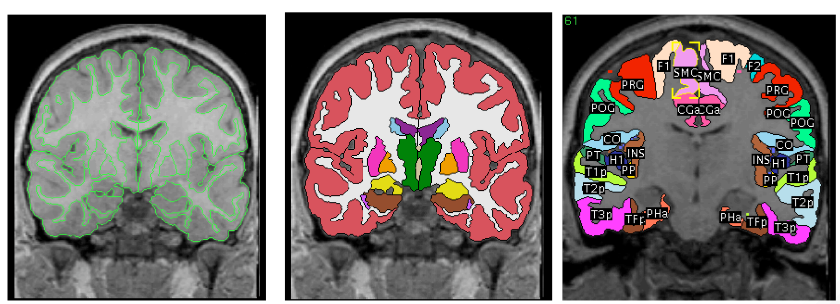
EEG investigations of steady state auditory evoked responses (frequency domain)





MEG investigations of cortical feature extraction and sensory gating mechanisms (time domain)

aMRI volumetric investigations of auditory and language cortex



Our Experimental Approach

Childhood is a moving target …

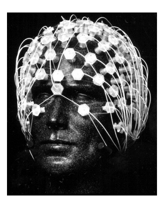
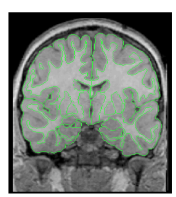
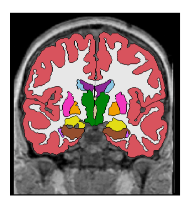
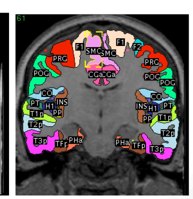
To reduce variability within and across groups, use age-matched children within a narrow age band.

What constitutes a control for autism?

Experimental protocols include no task, no requirement for overt response, and minimal compliance. In this way, we hope to elucidate between-group differences that correspond to neural mechanisms and not to attentional processes, compensatory strategies, or coping skills.

Whole brain, whole child …

To increase the power for elucidating the correspondence between structural and functional brain measures, we use a within-subject design wherever possible, and assess correspondence of brain measures to clinical and behavioral tests.


The Sample: UCI Autism Research Center
Dr. M. Anne Spence, Director

All children with autistic disorder (AD) were recruited from the large sample of children with AD, their siblings, and typically developing children provided by the UCI Autism Research Center. This sample contains many sets of MZ and DZ twins, both concordant and discordant for autism. Control children were recruited from the Center when possible, or from the UCI community.

The children are well-described:
- diagnostic (ADOS, ADI-R)
- neuropsychological (IQ, language)
- clinical (dysmorphology, pedigree)
- anatomical (MRI)
- DNA testing.

General Clinical Research Center at UCI

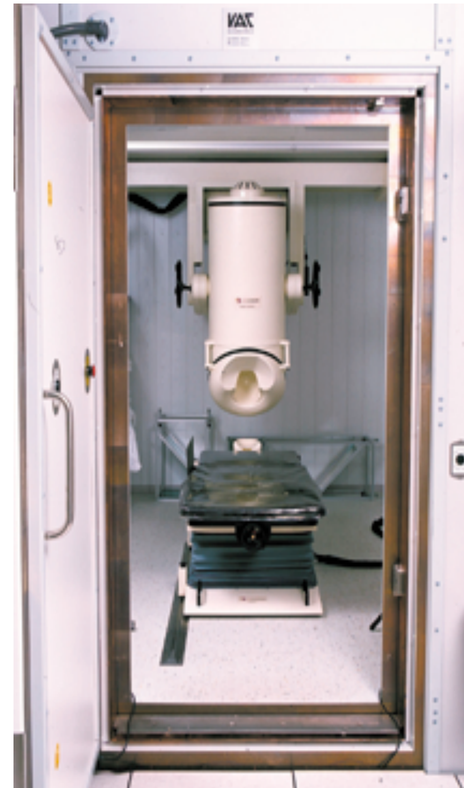
Neural Synchrony in the Cortical Auditory System

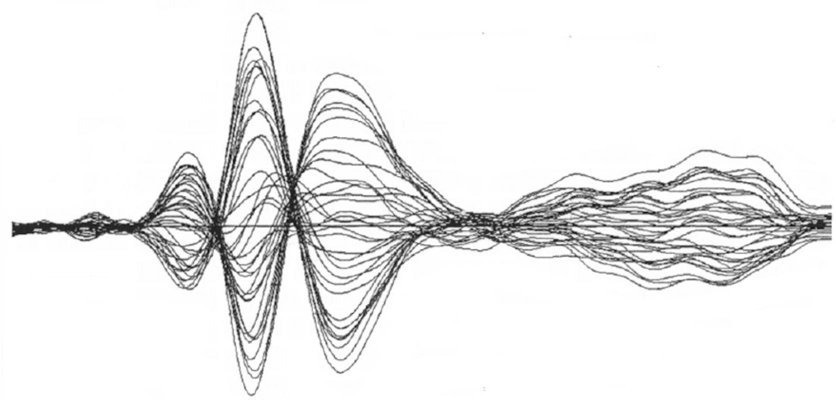
The temporal resolution of the auditory system is exquisite, with neural systems that decode features in the acoustic signal capable of submillisecond resolution.

The high level of resolution in auditory cortical systems provides the capability for decoding fine-grained fluctuations in sounds, critical to speech perception.

Magnetoencephalography (MEG)

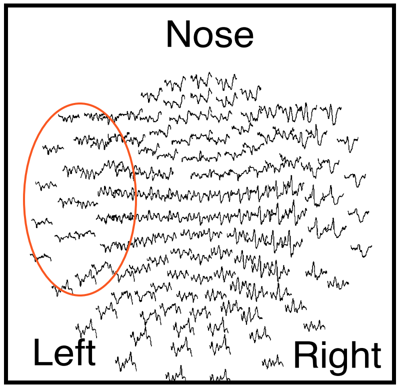
- Recording of the small magnetic field associated with current sources in the brain using SQUID devices.
- Millisecond temporal resolution
- Post-synaptic, dendritic flow
- Synchronized response of populations of neurons
- Event related or steady state
- Well suited for studying structures in the sulcal folds – sensory areas
- Well suited for studying synchrony across brain areas
- Recording is entirely non-invasive and silent

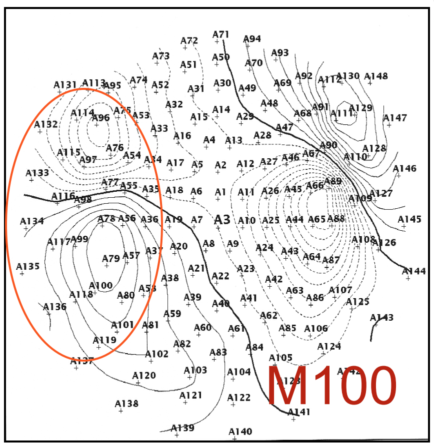


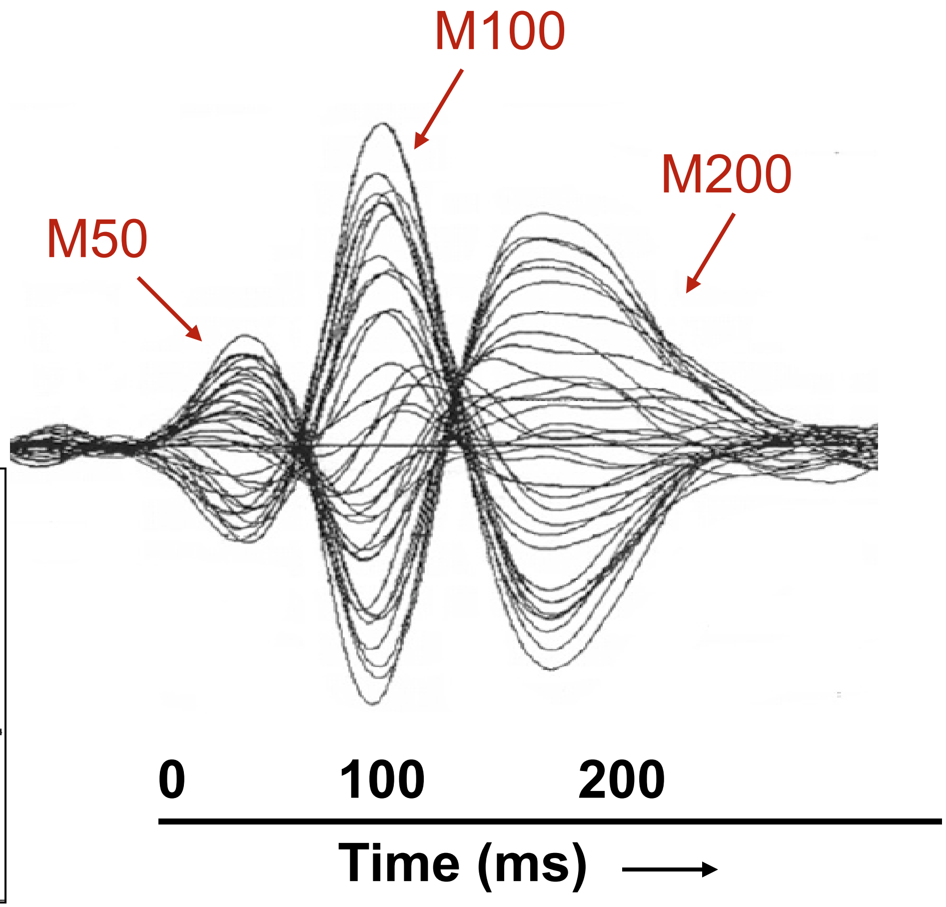


Neuromagnetic Auditory Evoked Field

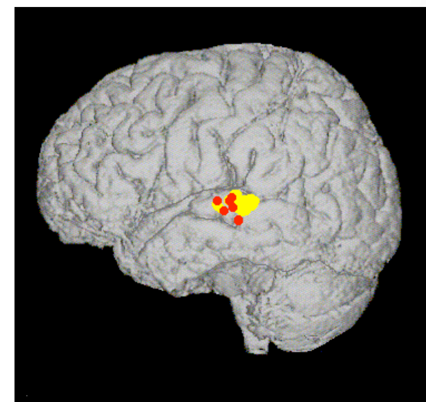
Discrete Stages in Cortical Processing in Left and Right hemispheres on a Child-by Child Basis







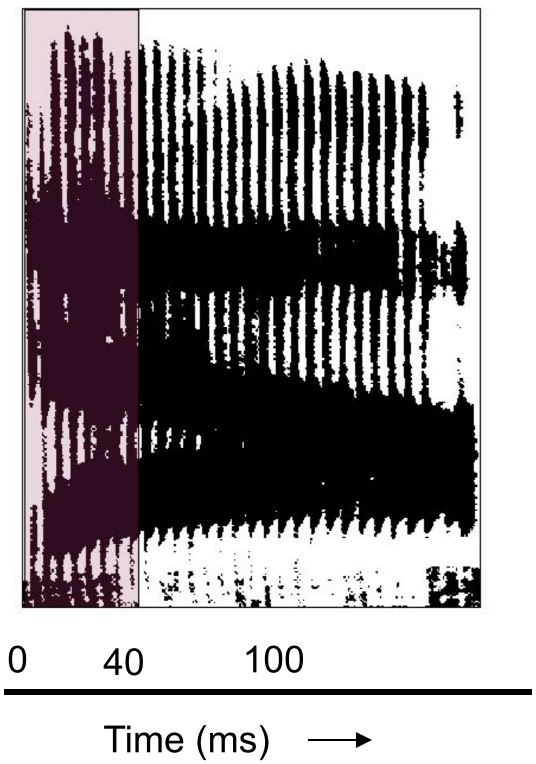
M100 localizes to auditory cortex

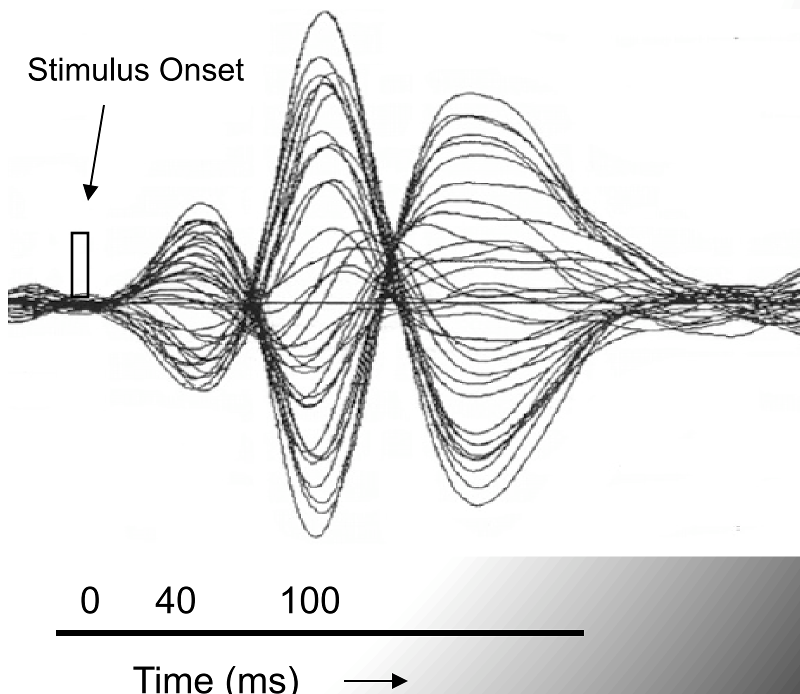


A prototype auditory evoked neuromagnetic field detected by MEG; 37 channels with y-scale representing evoked response magnitude in units of femtotesla (fT) are shown collapsed on the same horizontal time axis.

MEG Investigations of Temporal Acuity in the Processes Underlying the Auditory M100 Component

Gap detection thresholds measured psychophysically correspond to speech perception acuity, indicating that similar or overlapping neural processes are employed both in detecting brief silent gaps and in resolving the fine structure of the speech signal.

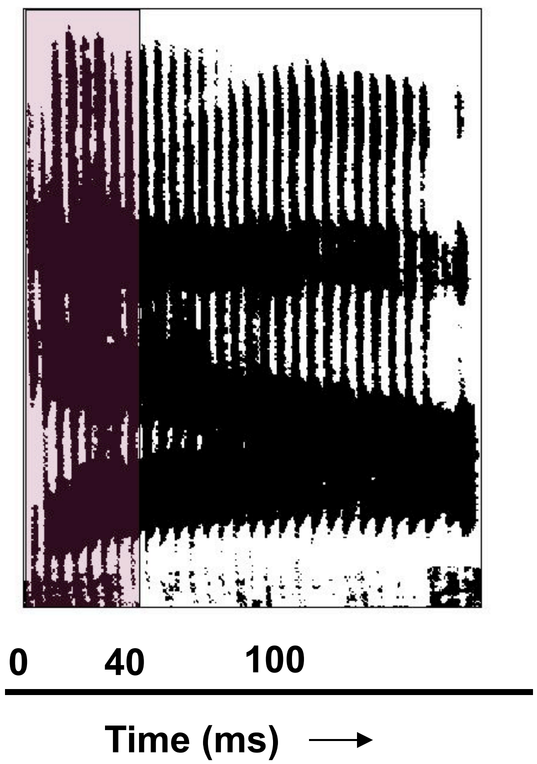


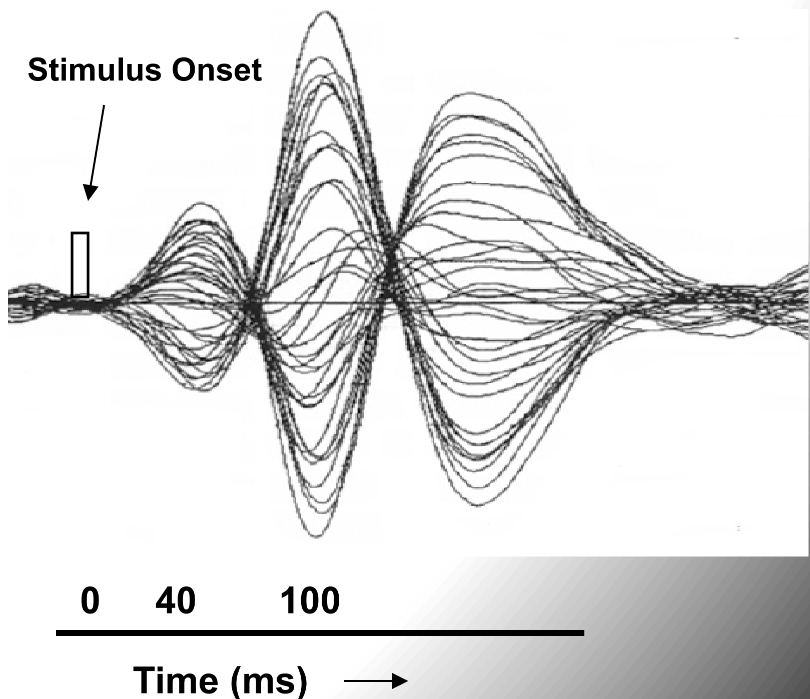


Temporal Resolution of the Auditory M100: Gap Detection Experiments

The investigation: we know that M100 is sensitive to the presence of a stimulus within a brief, finite (25-40 ms) integrative window.
What are the lower limits of the resolution for brief discontinuities – or the absence of a stimulus – within that window of integration?

Gage and Roberts, 2000



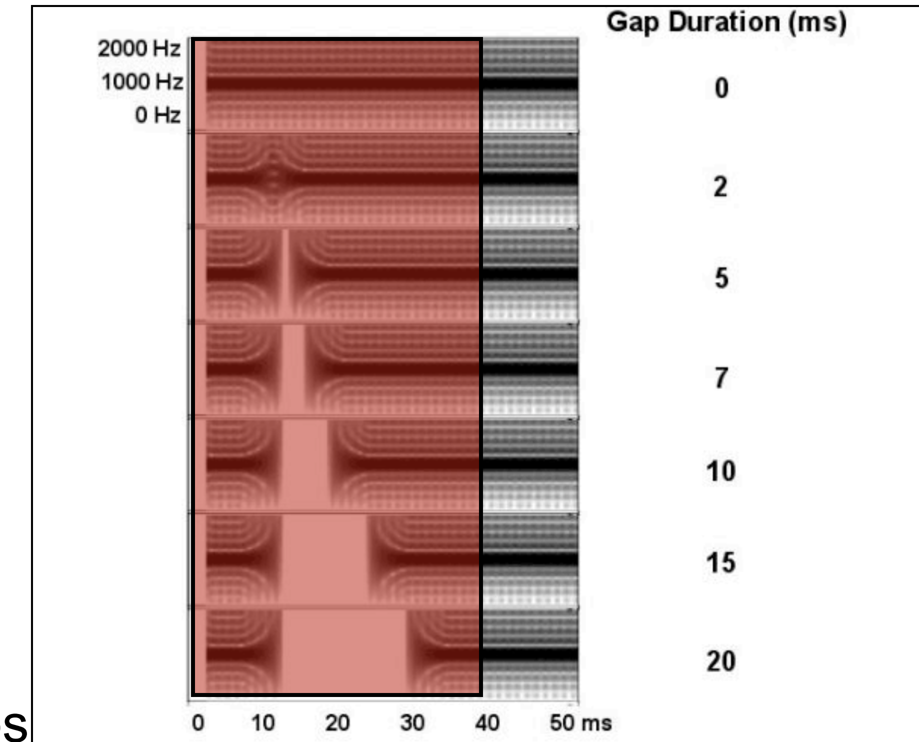


Temporal Resolution of the Auditory M100: Gap Detection Experiments

How sensitive is the M100 to fine-grained temporal discontinuities in sounds?

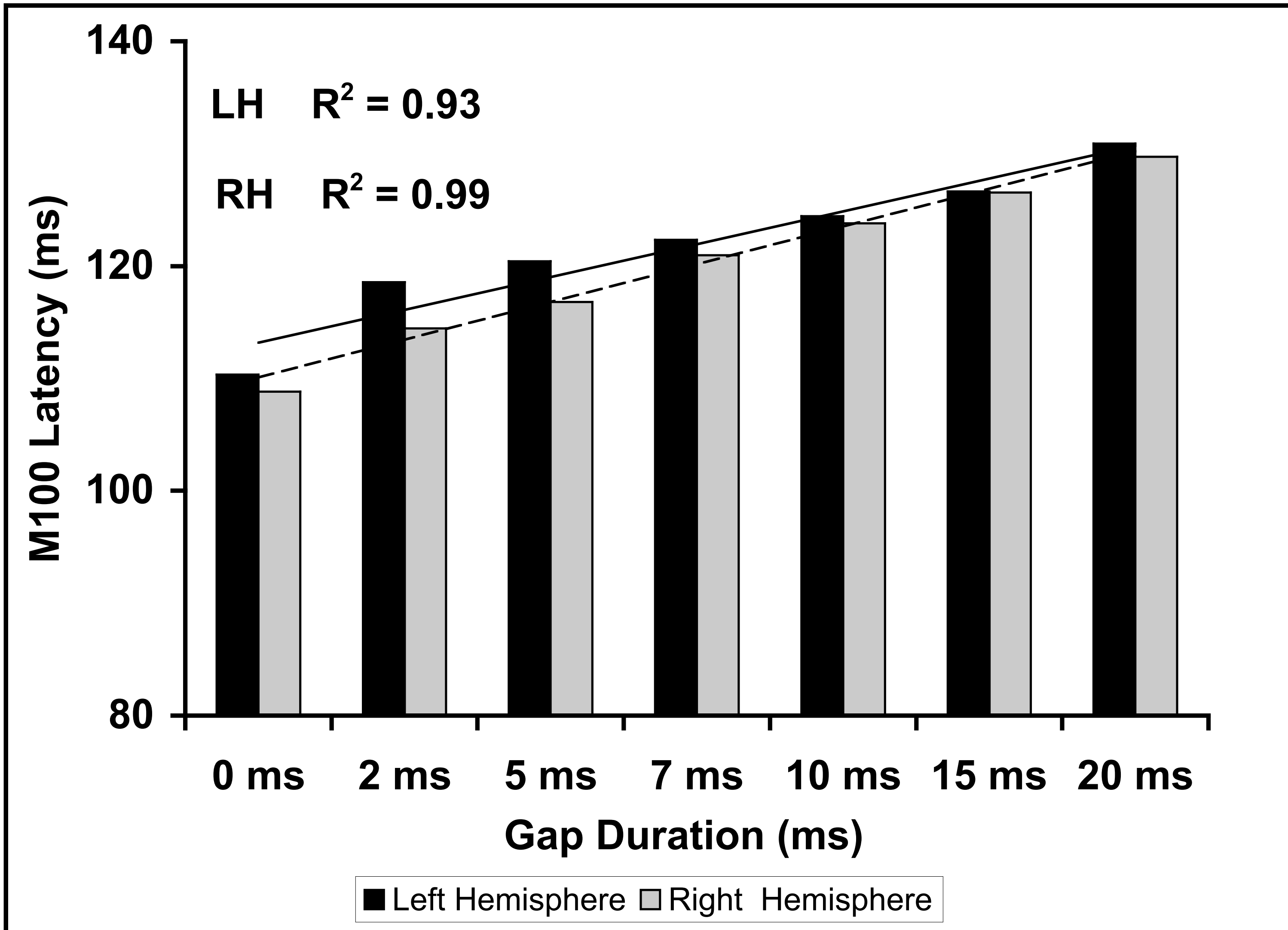
We address this question by inserting brief gaps of silence at +10 ms post stimulus onset and measuring M100 modulation as a function of gap duration. N=12 (7 male) right handed adults.

In a second condition, we inserted gaps at +40 ms post onset. Here we predicted that M100 would not be modulated by gaps of silence because the gaps were inserted outside the integrative window.



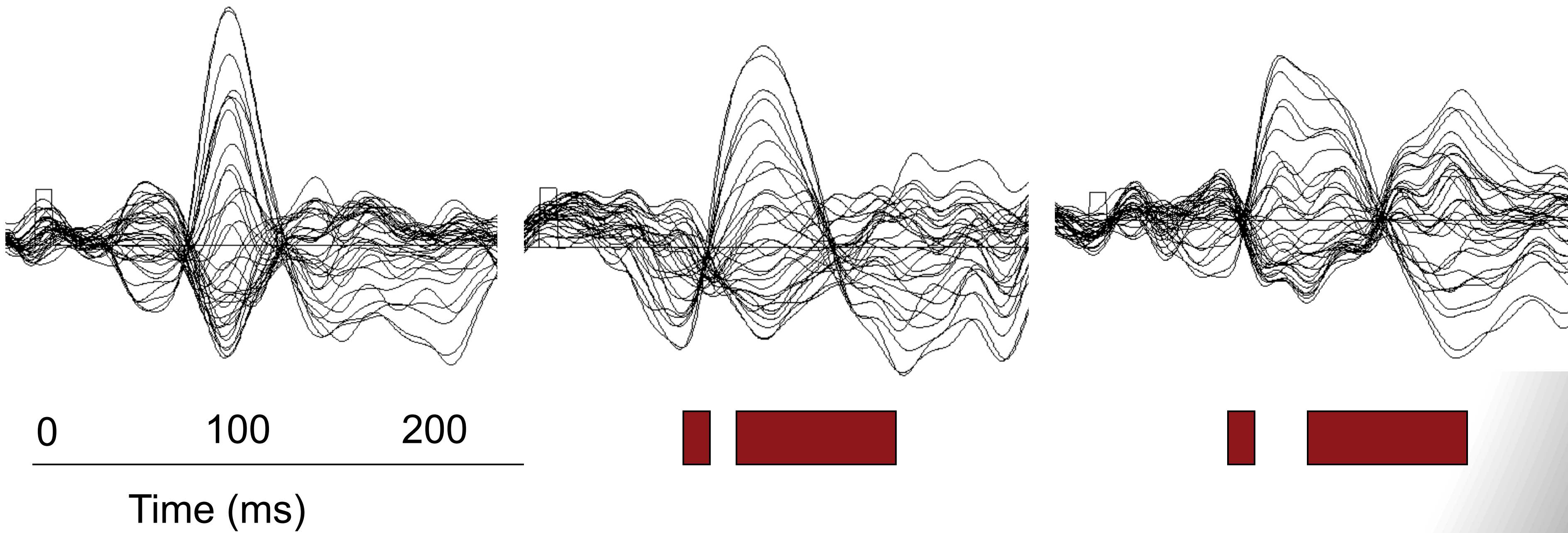
Temporal Window
of Integration
(~25-40 ms)
Gage & Roberts, 2000

Results for Adults: M100 Latency is modulated by brief discontinuities in tones



Gage, Roberts, & Hickok, 2006

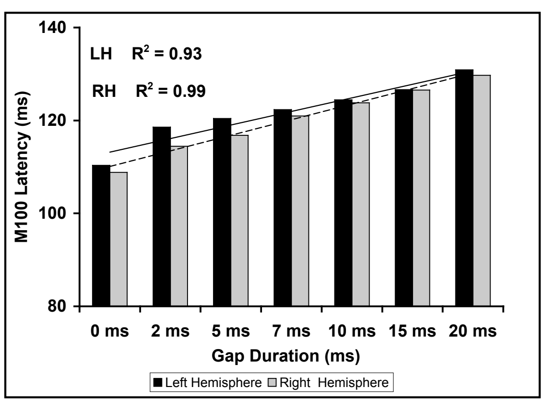
Results for Adults: Effect of gap onsets and offsets on neuromagnetic field morphology



no gap

10ms gap

20ms gap



Temporal Resolution of the Auditory M100: Gap Detection Experiments with Children

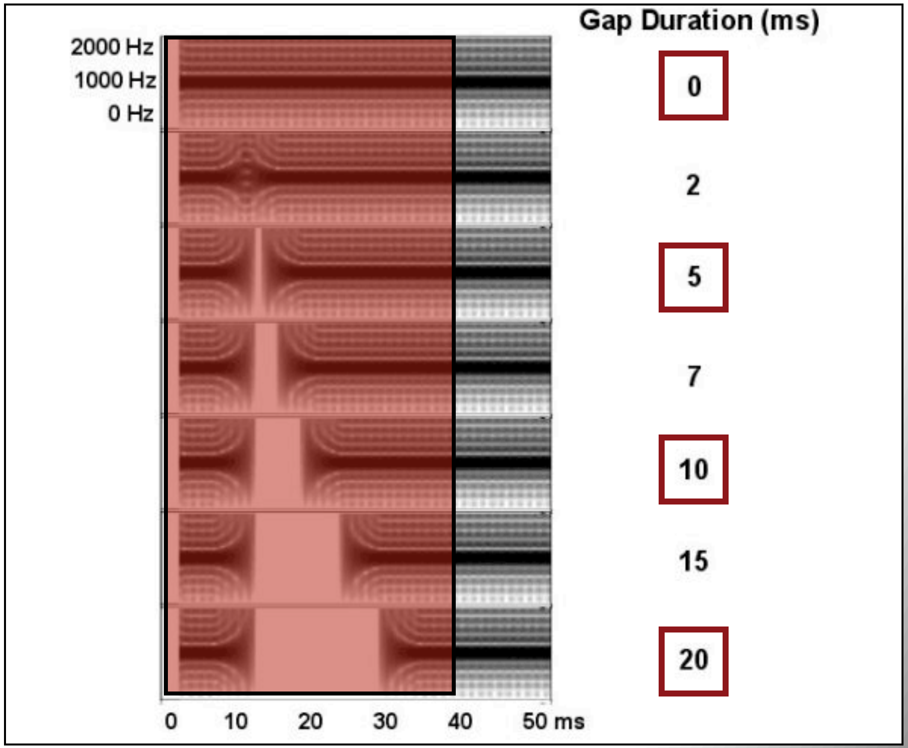
N=17 (2 female) children with AD
M 10,11 yrs (1,7), M VIQ 70

N=17 (2 female) TD controls + SIBs not on the spectrum M 10,4 yrs (1,7)

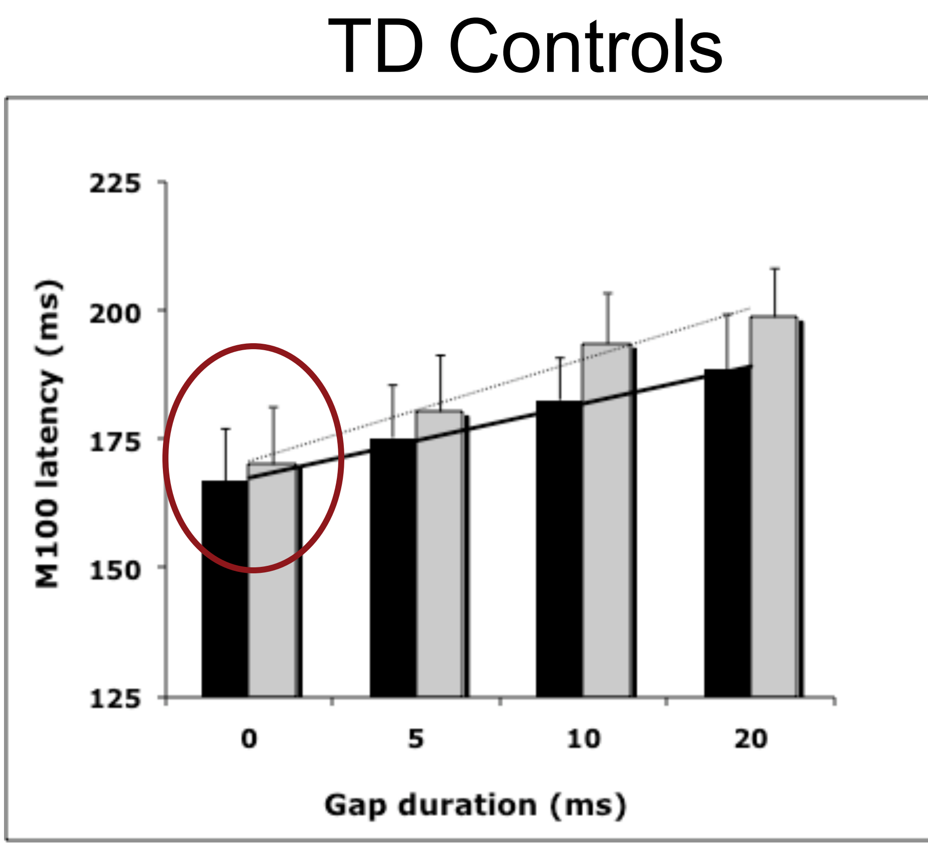
Stimuli consisted of 1000 Hz tones containing brief discontinuities (gaps) of 0, 5, 10, 20, and 40 ms, presented binaurally at 70 dB SPL

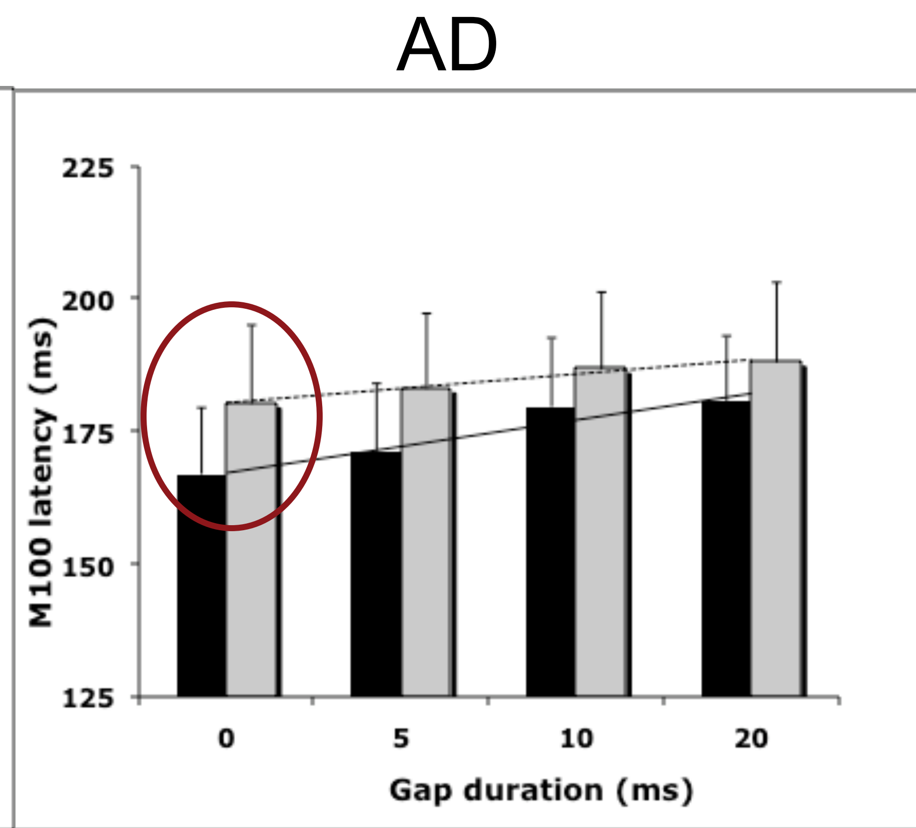
Stimuli were presented 100 times each, interleaved, in pseudorandom order.

Latency of the M100 served as the dependent measure



M100 Latency modulation by gaps of silence



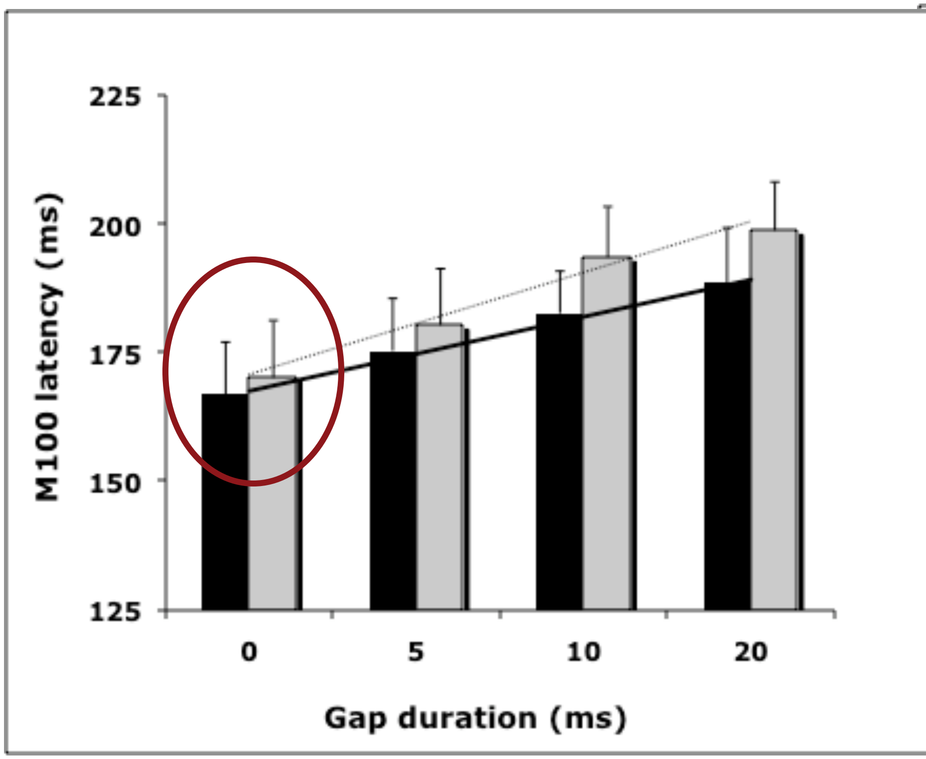


Left hemisphere: R^2 0.99, 7.2
Right hemisphere: R^2 0.98, 9.9

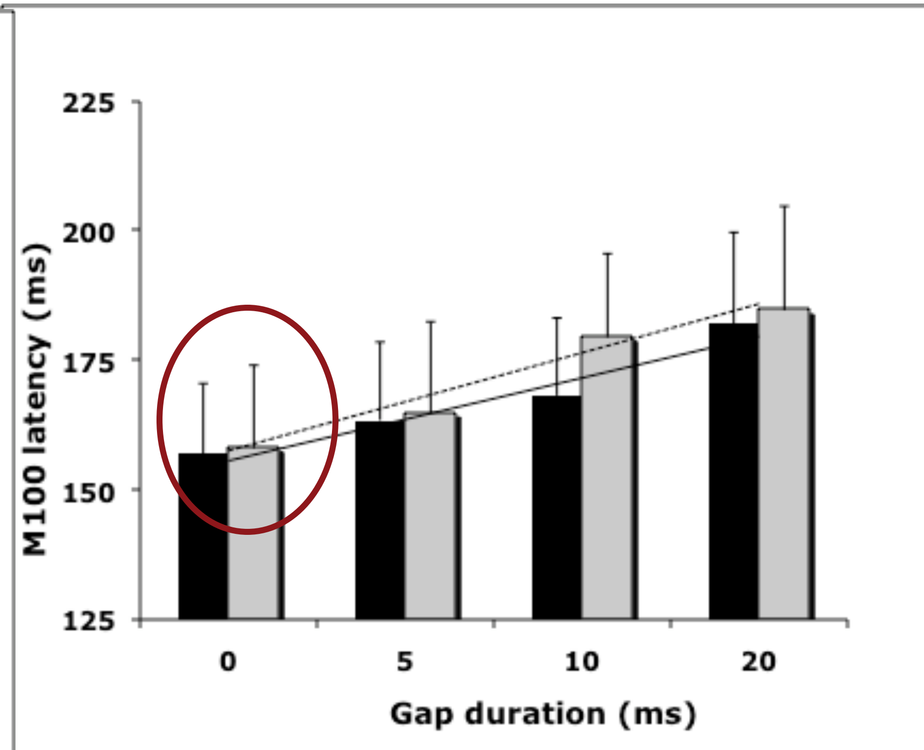
Left hemisphere: R^2 0.93, 5.0
Right hemisphere: R^2 0.97, 2.7

M100 Latency modulation by gaps of silence

TD Controls



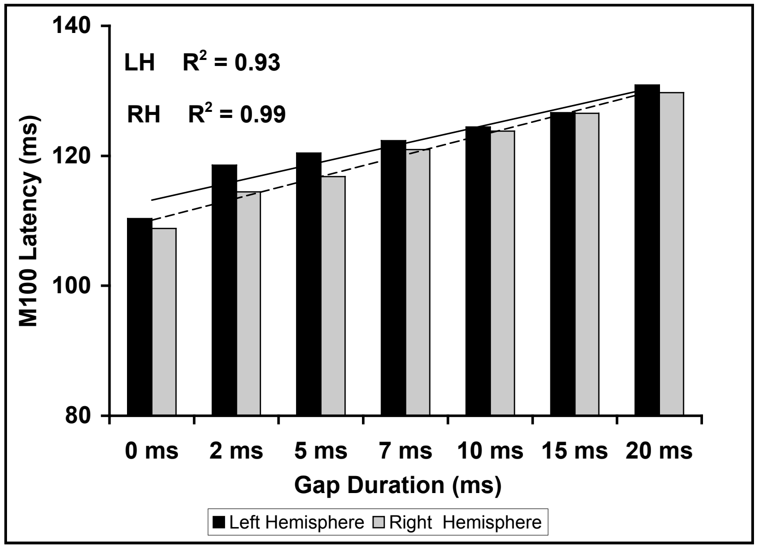
SIBs



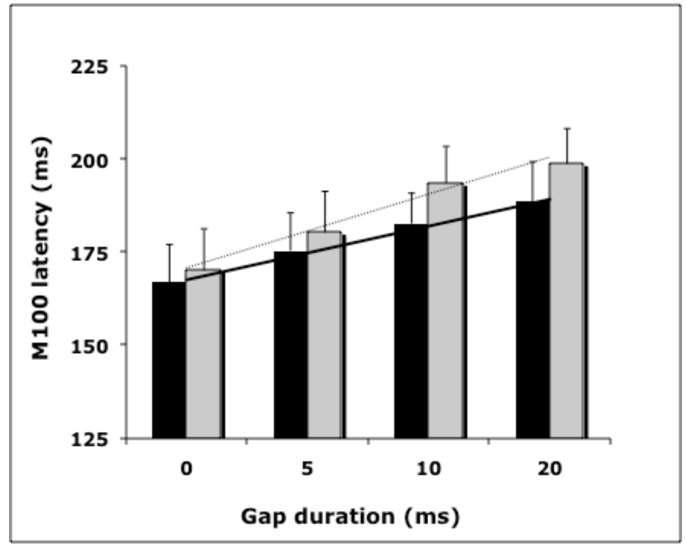
Left hemisphere: R^2 0.99, 7.2
Right hemisphere: R^2 0.98, 9.9

Left hemisphere: R^2 0.93, 8.0
Right hemisphere: R^2 0.97, 9.5

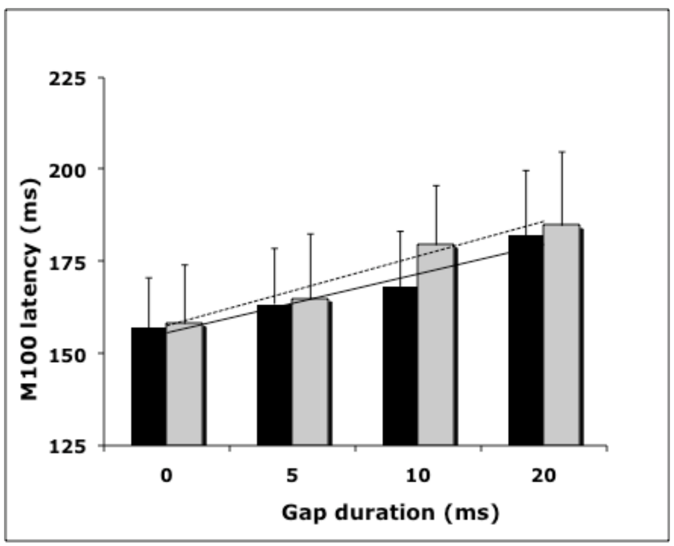
Adults



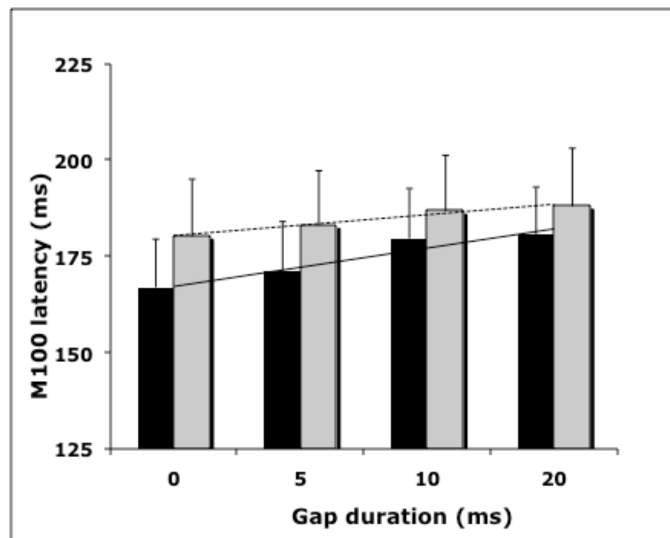
TD Controls



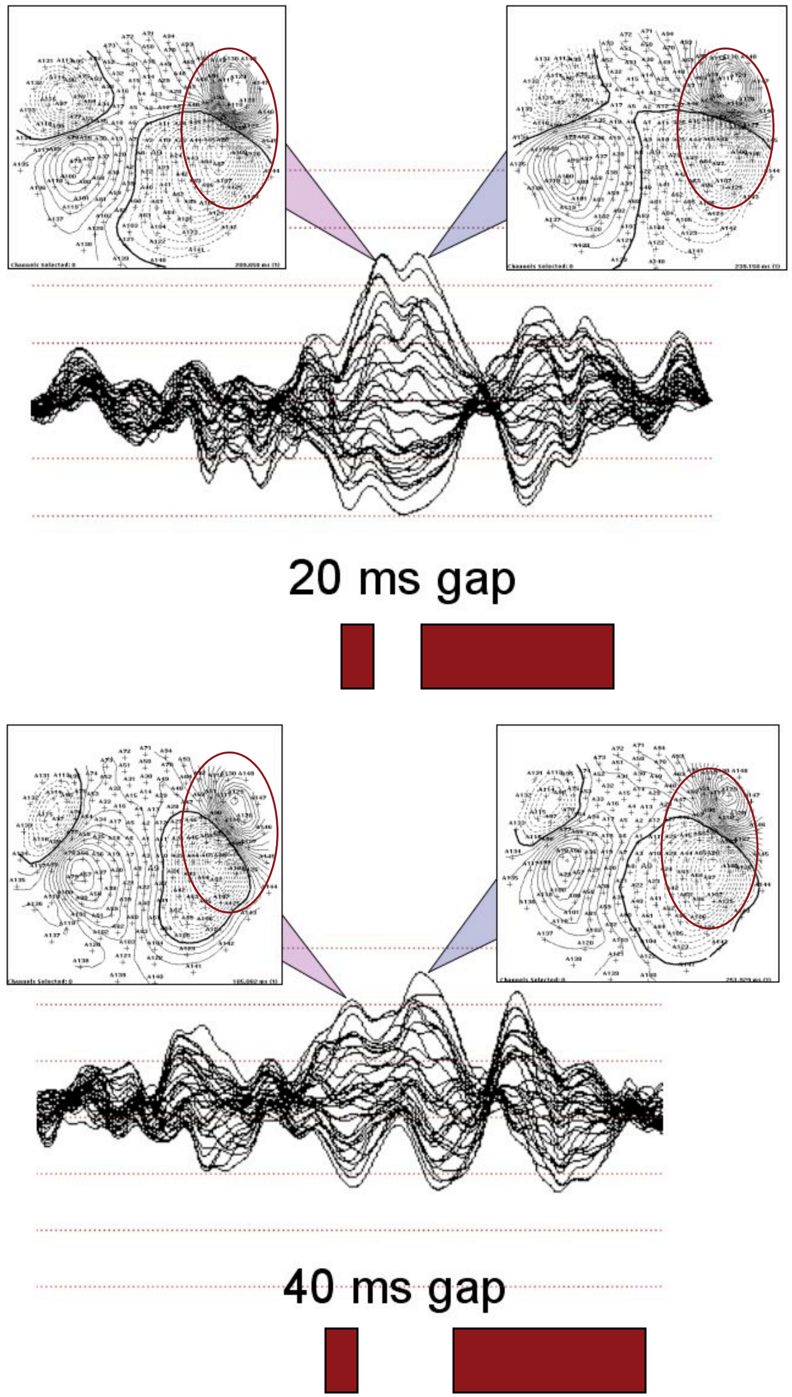
SIBs



AD

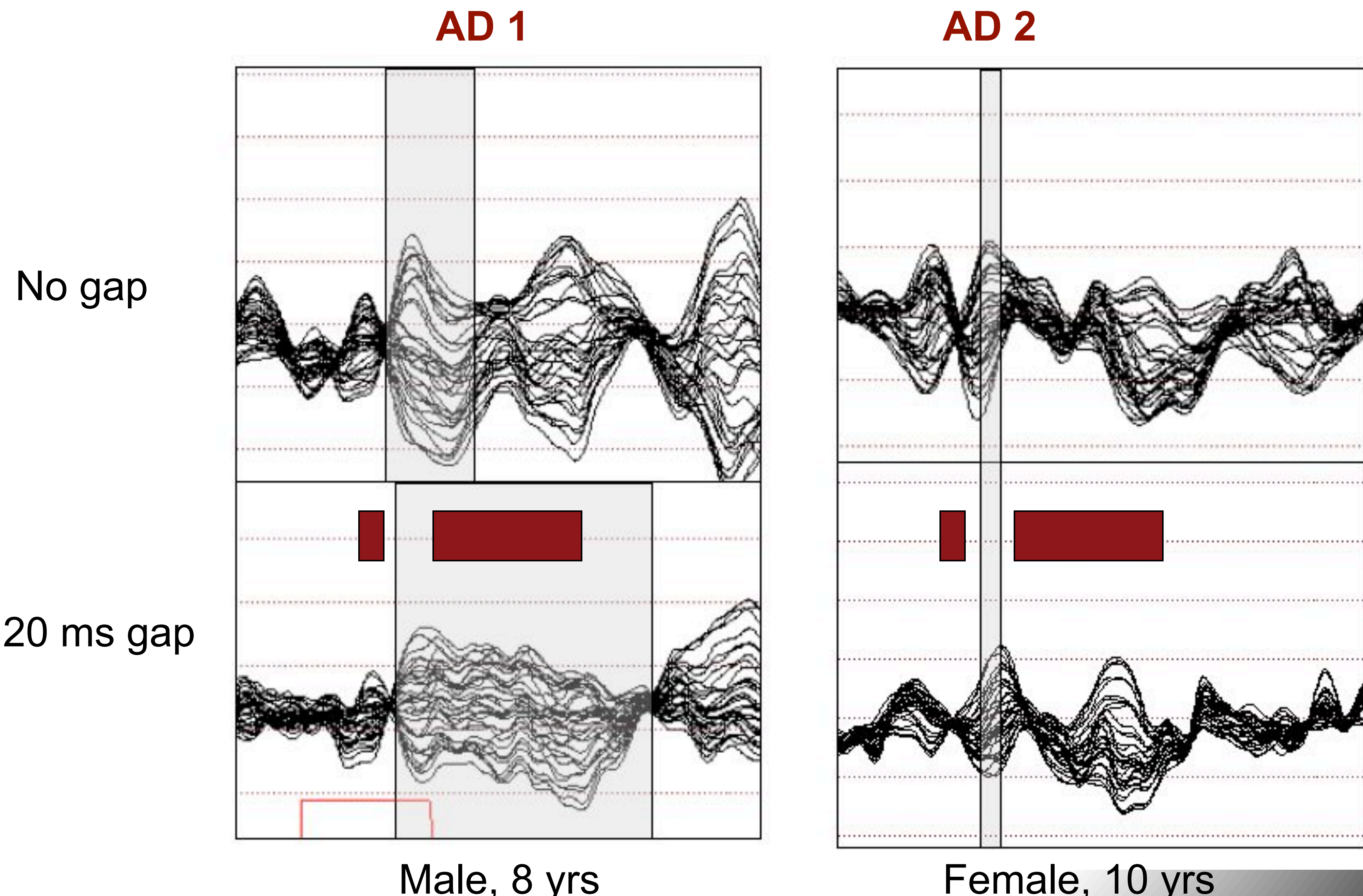


TD

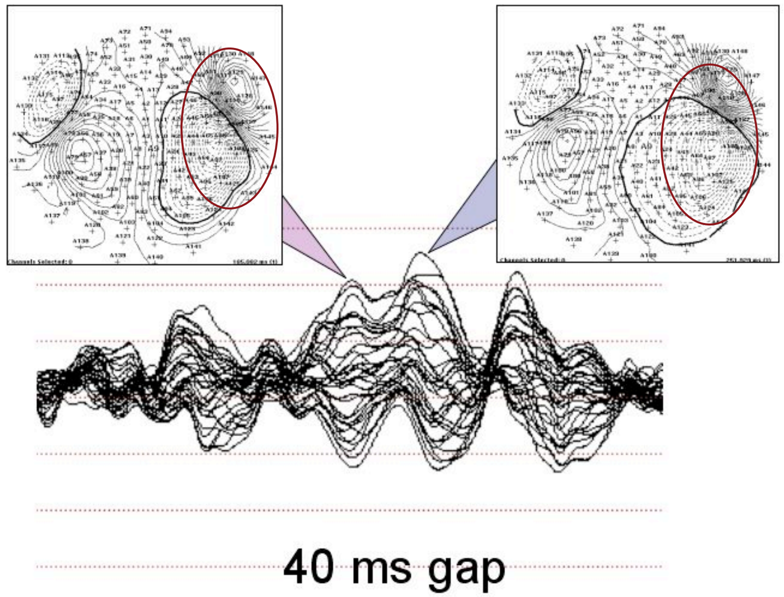


Auditory evoked field (right hemisphere) for a Control (male, 11 yrs) showing effect of tone onsets/offsets about the gap.

AD: two general effects are evidenced in the morphology of the auditory evoked field – an extended prolongation (AD 1) or no prolongation (AD 2)

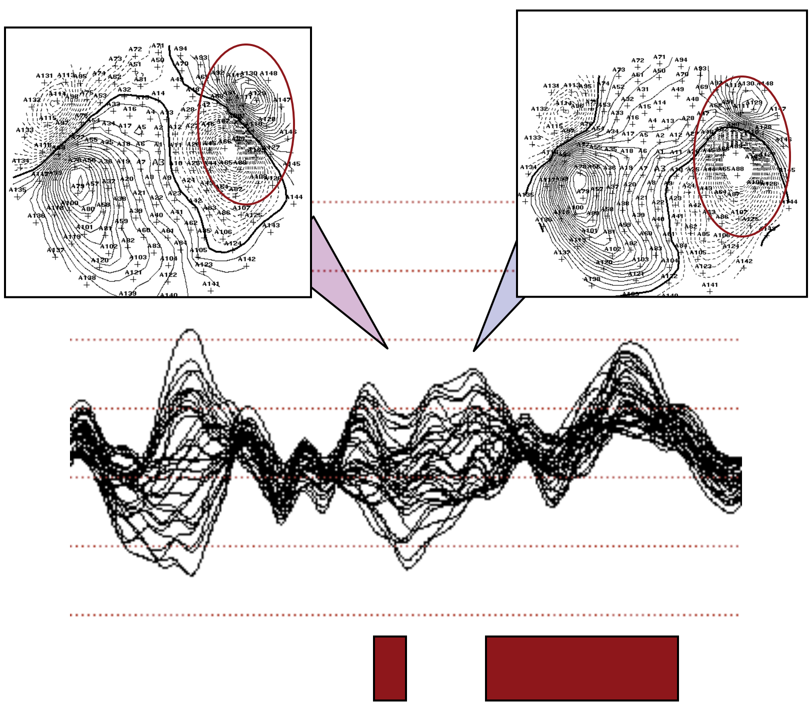


TD

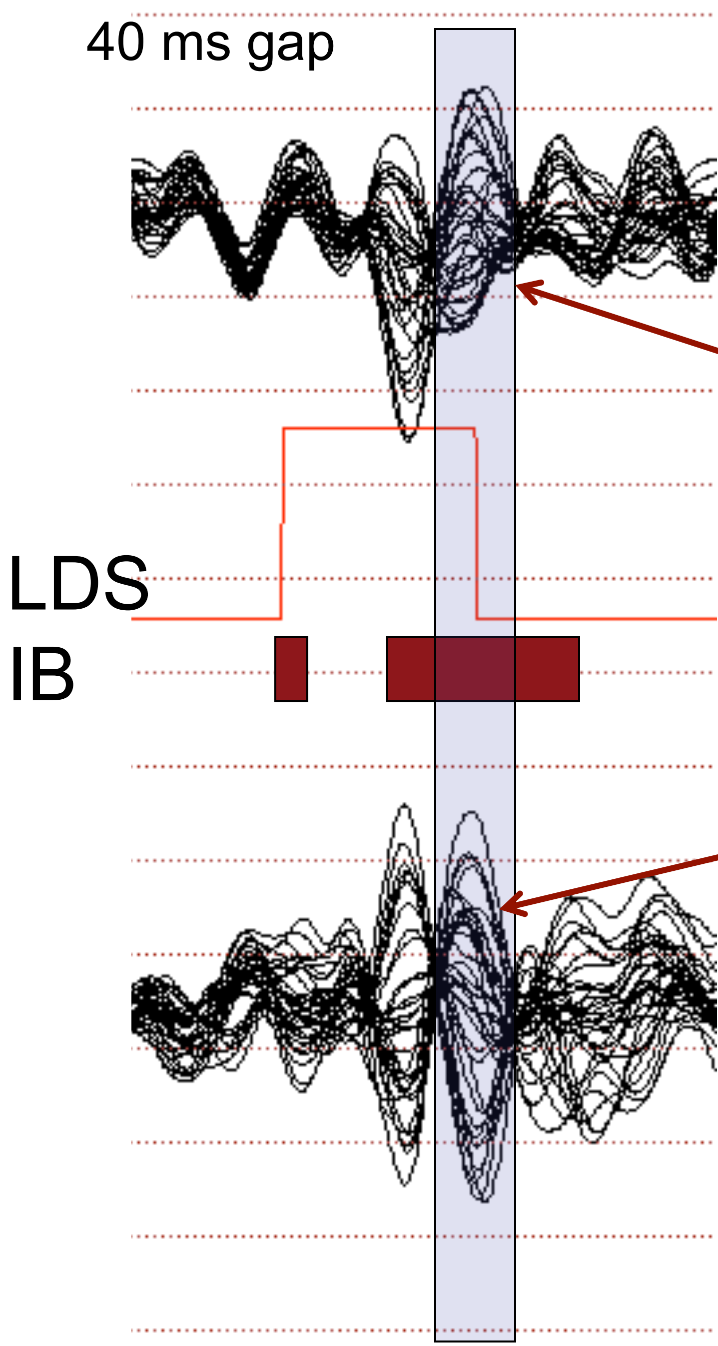


Auditory evoked field (right hemisphere) for a Control (male, 11 yrs) showing effect of tone onsets/offsets for the 40 ms gap.

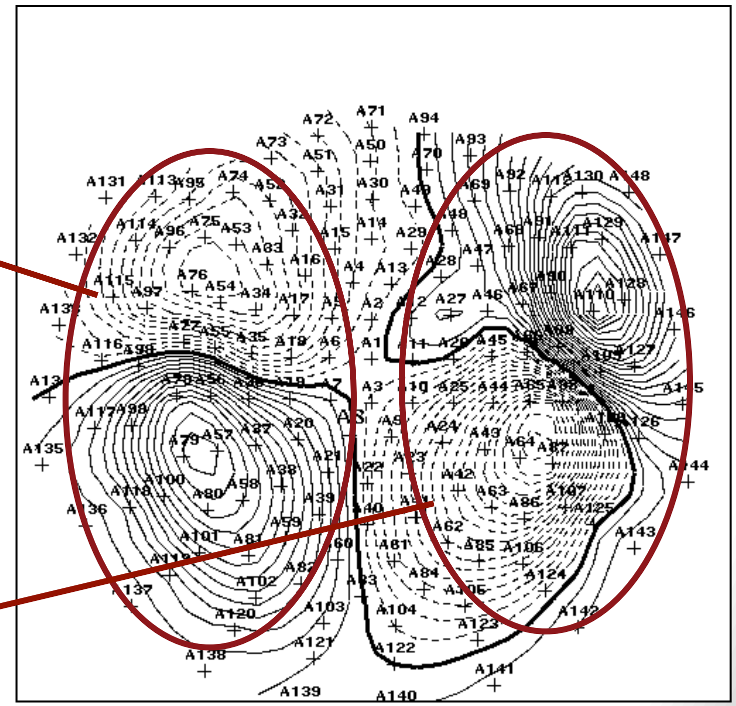
SIB

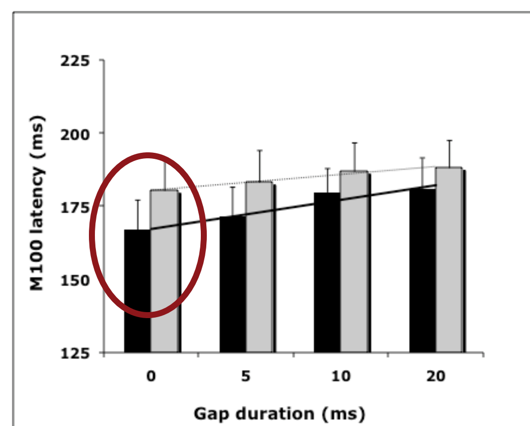


Auditory evoked field (right hemisphere) for a Sibling (male, 8 yrs) showing effect of tone onsets/ offsets for the 40 ms gap.

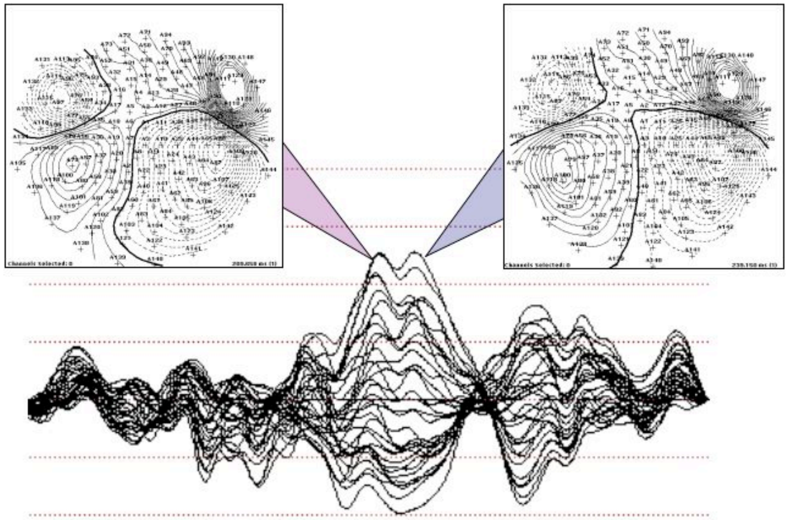


Auditory evoked fields for a Sibling (male, 12 yrs, language delayed) for the 40 ms gap.

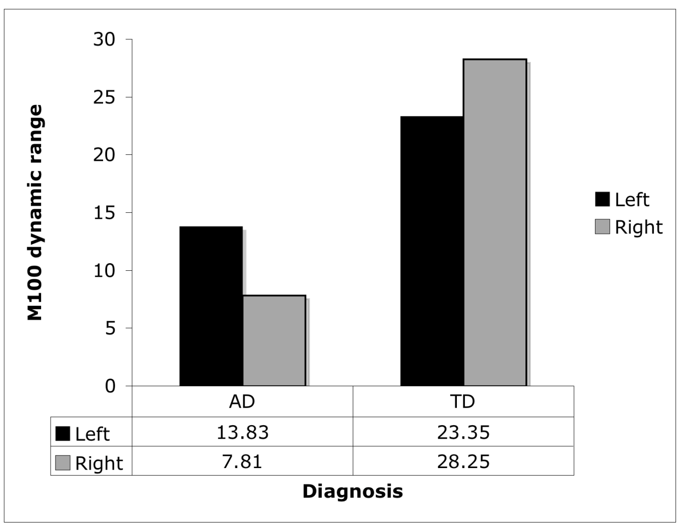




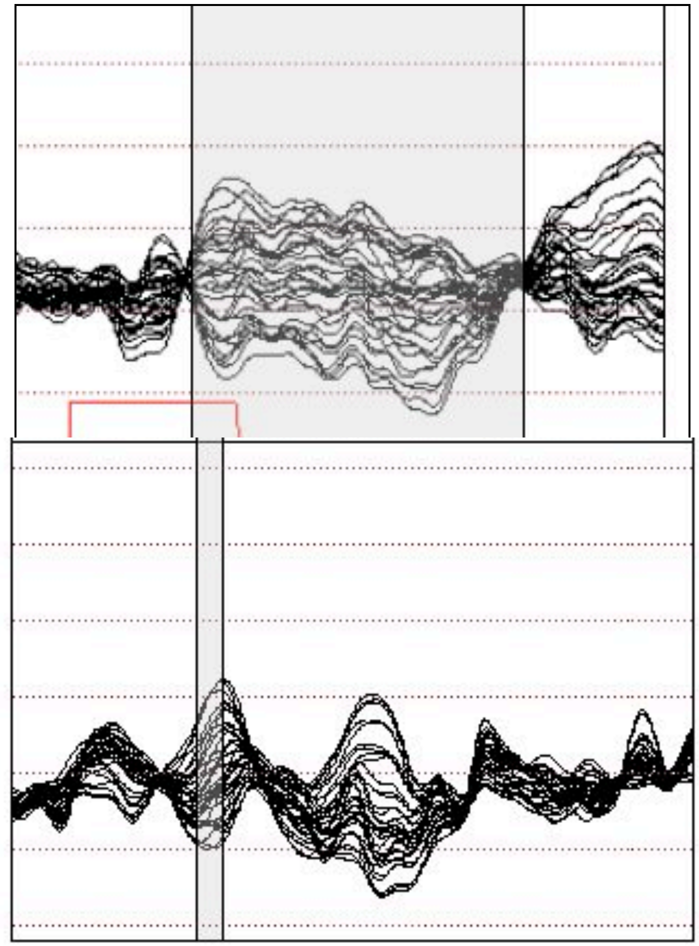
Neural synchrony in auditory cortical processes underlying both gap detection and speech perception are impaired in autism



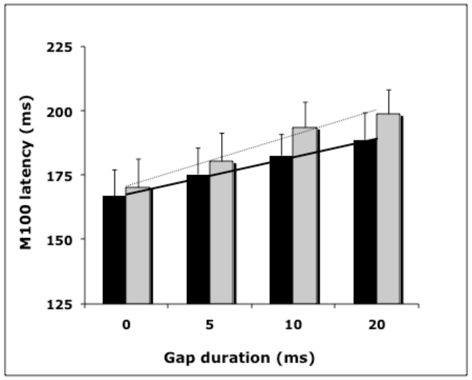
20 ms gap

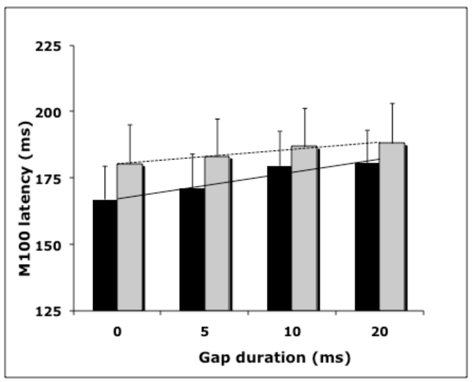


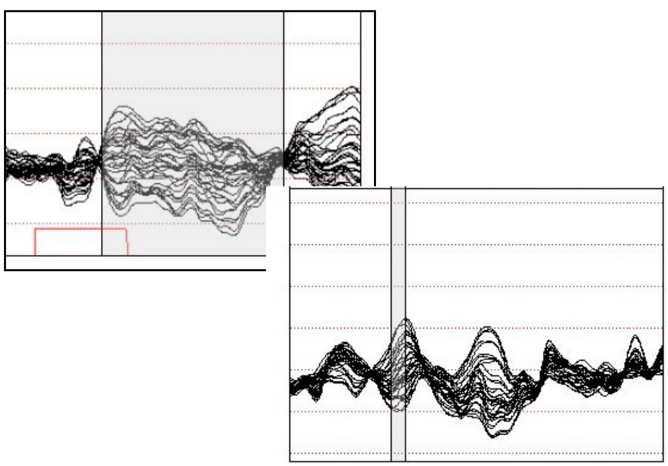
	AD	TD
Left	13.83	23.35
Right	7.81	28.25



Summary and Conclusions



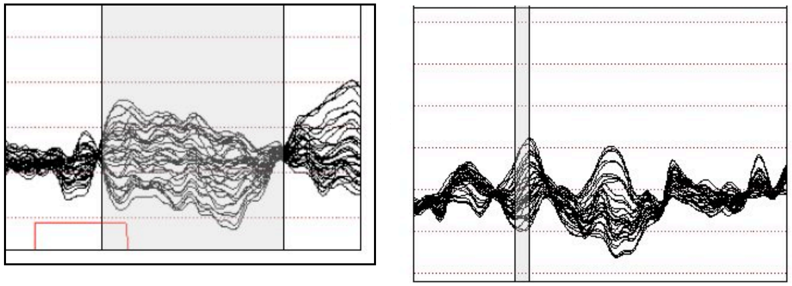




- Typically developing children show M100 modulation by brief discontinuities in sounds in a manner similar to adults
- Children with autism show reduced resolution of these discontinuities, especially in the right hemisphere
- Children with autism show asynchrony in M100 peaks in left and right hemispheres
- Some, but not all, siblings of children with autism show typical M100 modulation

Future Directions

- What is the correspondence of M100 findings to neuropsychological assessments, language outcomes, and clinical symptomology?
- Do the diverse patterns of response in children with autism correspond to speech perception deficits? Or sound sensitivity?



- Sibling data motivate new studies with our geneticist colleagues to investigate genetic loci that may shed light on shared brain function

A Team Effort …

UC Irvine
M. Anne Spence, PhD
Kathryn Osann, PhD
Lisette Isenberg
Paul Fillmore

Scripps Green Hospital, La Jolla
Shirley Otis, MD
Lacey Kurelowech
Patti Quint

Acknowledgements

We wish to thank the children and their parents for participating in this research

The National Alliance for Autism Research
The M.I.N.D. Institute at UC Davis
National Institute of Health R21DC 7236
(NMG)

National Institute of Health P01HD 35458
(MAS)