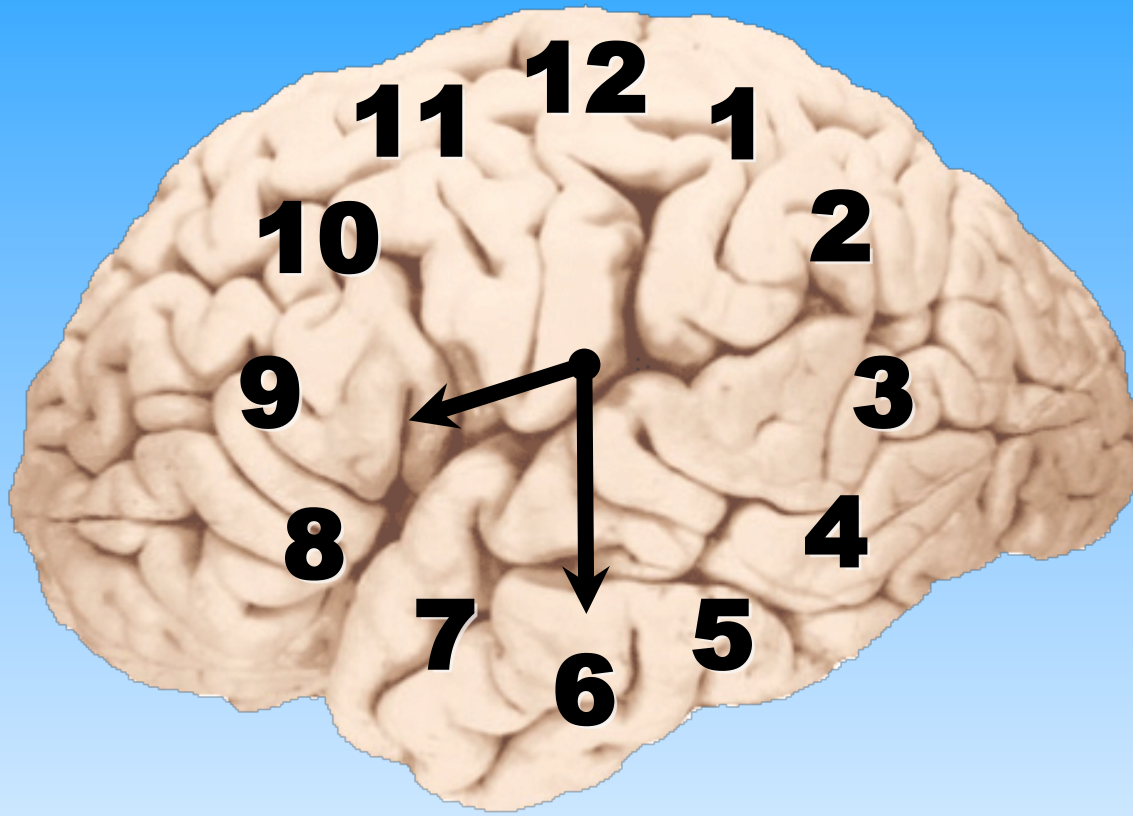
Understanding the Neurobiological Basis of Language is a Matter of *Time*



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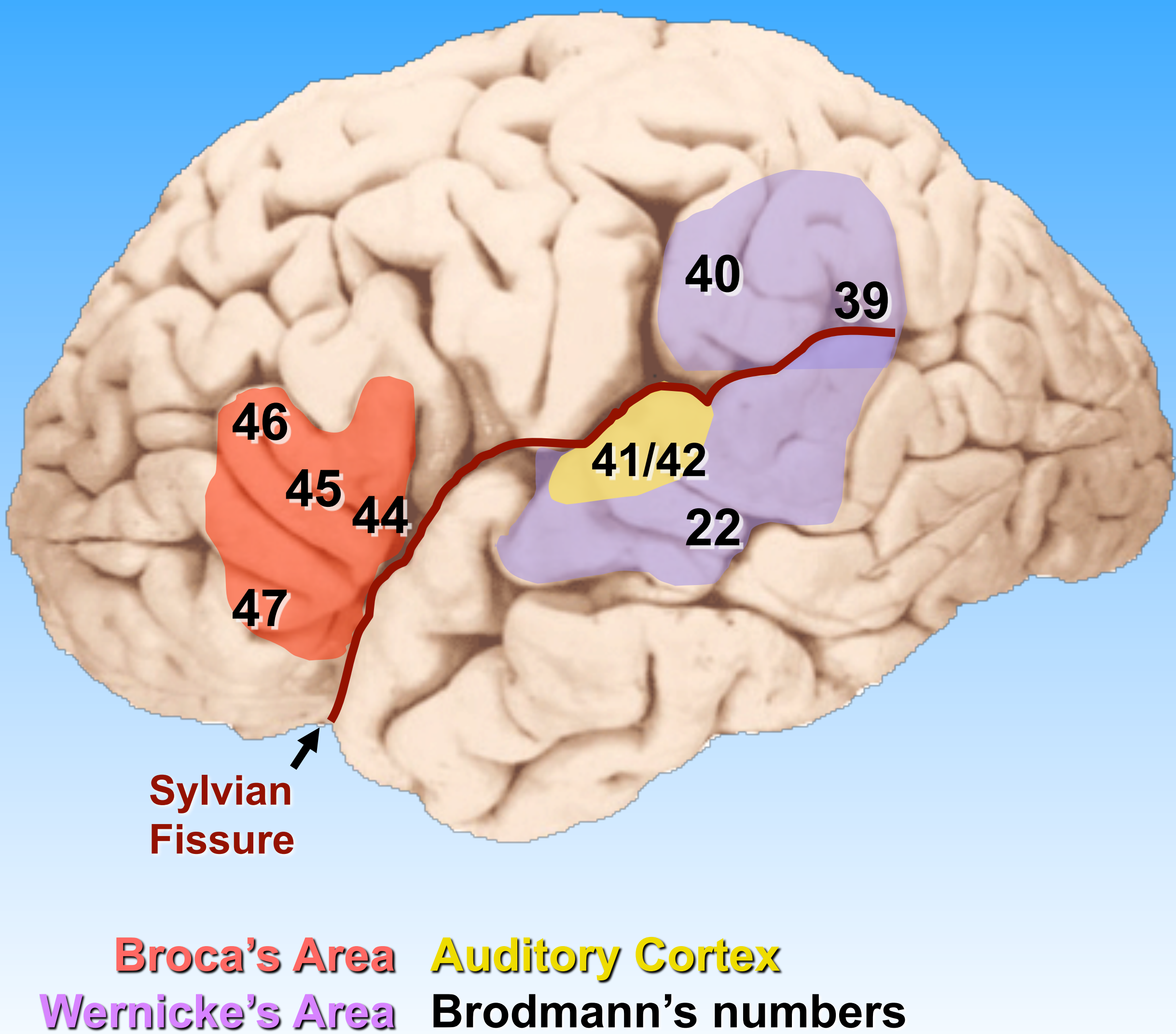
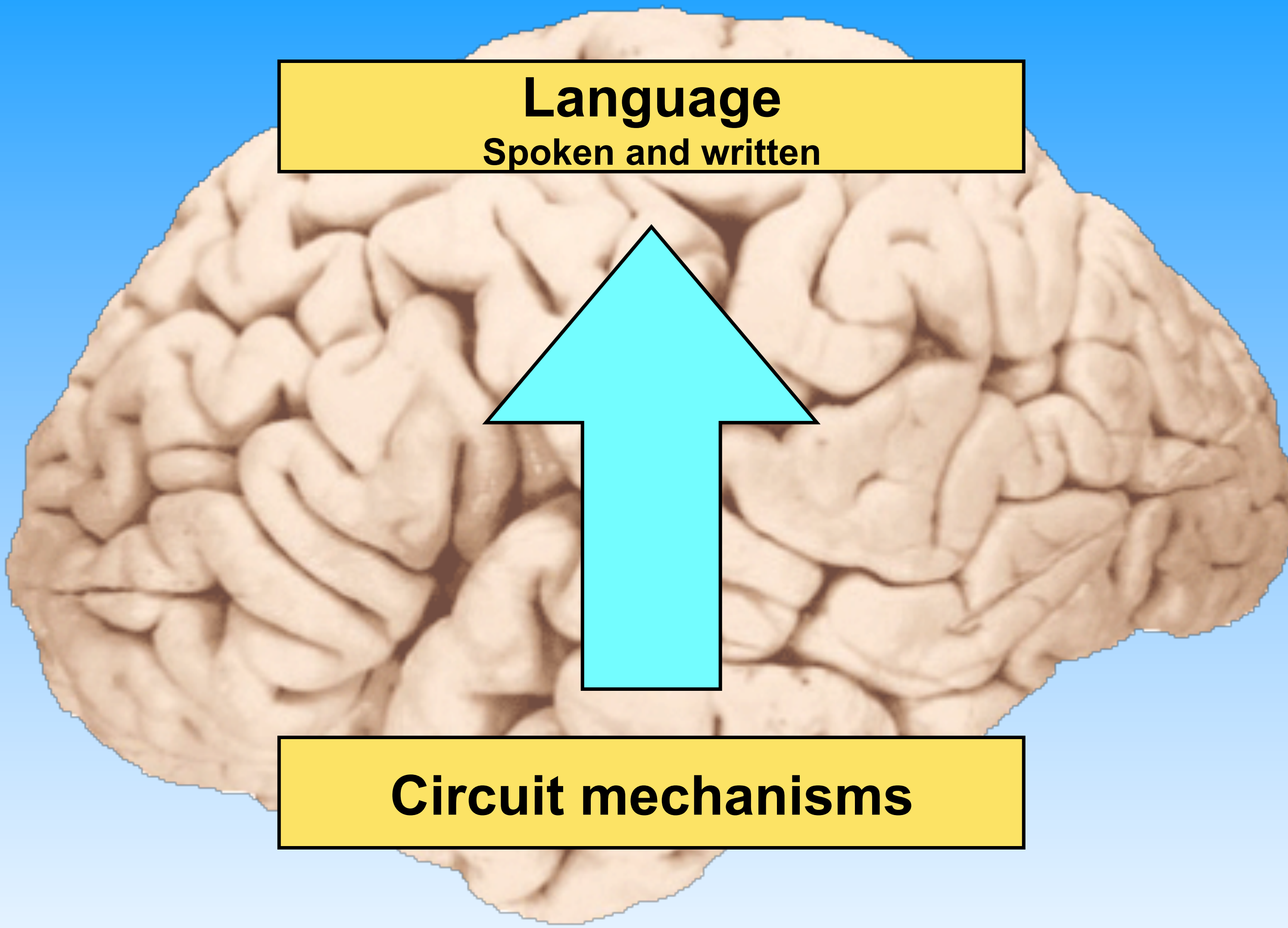
Research funded by NIH and NSF

Neurobiology of Language



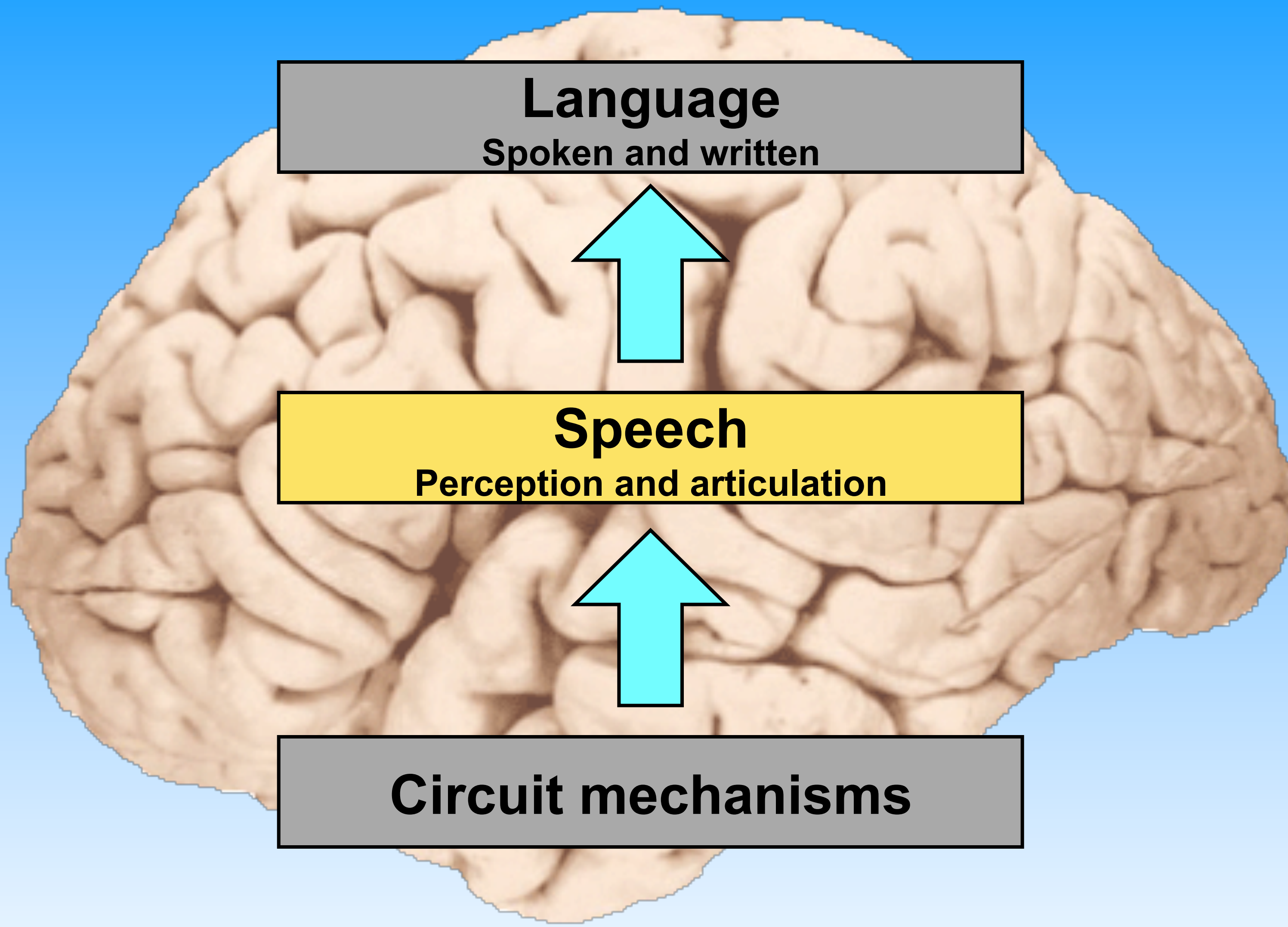
- Language is uniquely human. As such, it has been difficult to apply the majority of systems neuroscience techniques to the study of human language.
- Traditionally, what we know about the neural basis of language has been derived primarily from observing the effects of lesions to specific areas of the brain.
- More recently, the advent of functional neuroimaging technologies has revolutionized our ability to study brain activation patterns generated by language tasks.

Neurobiology of Language



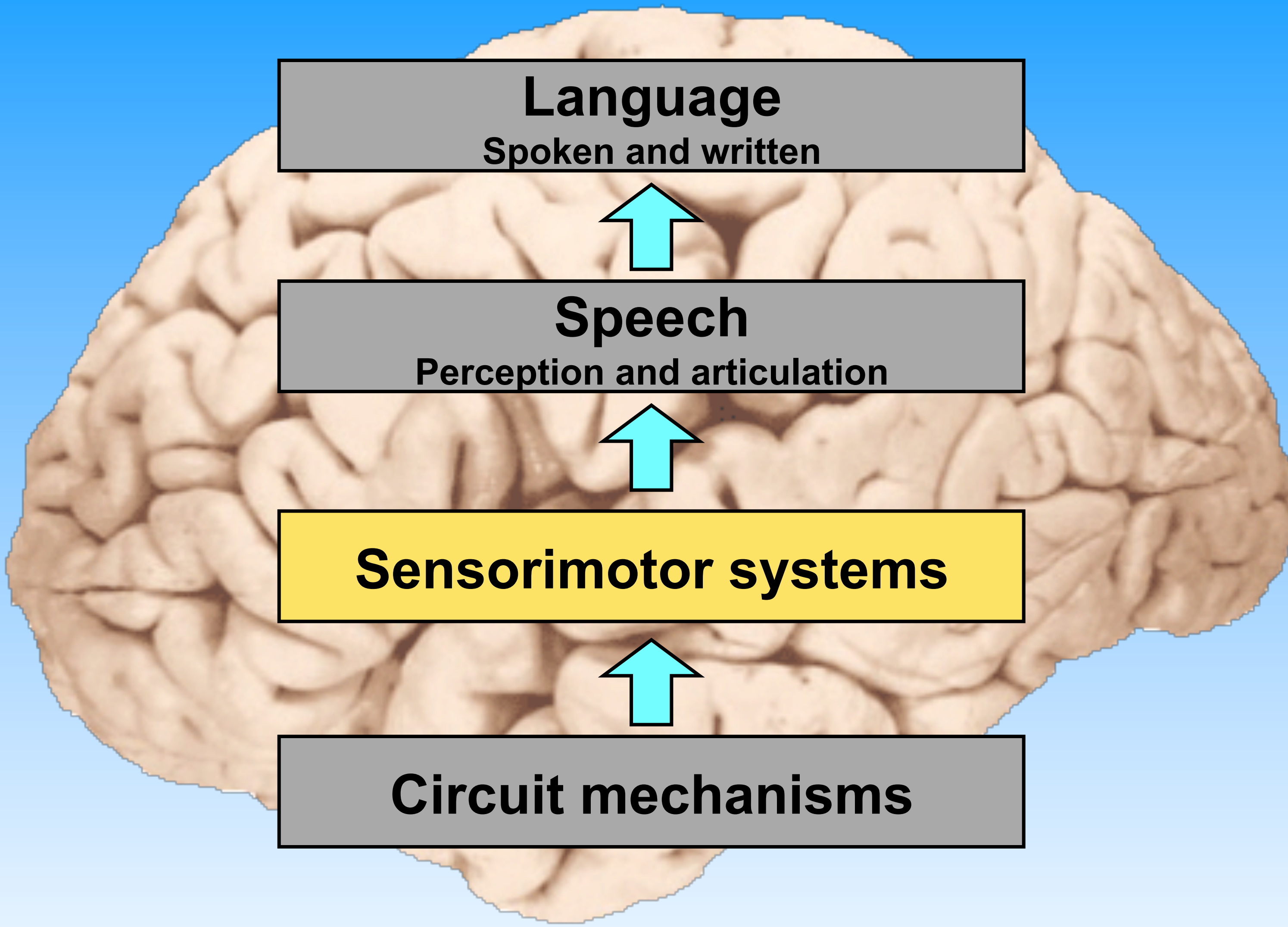
Despite these advances, it remains difficult to connect the study of cyto-architectural regions involved in language, with the study of neural circuitry

Neurobiology of Language



**We posited that rather than focusing on language, per se,
It would be more productive to focus on the speech signal itself.**

Neurobiology of Language

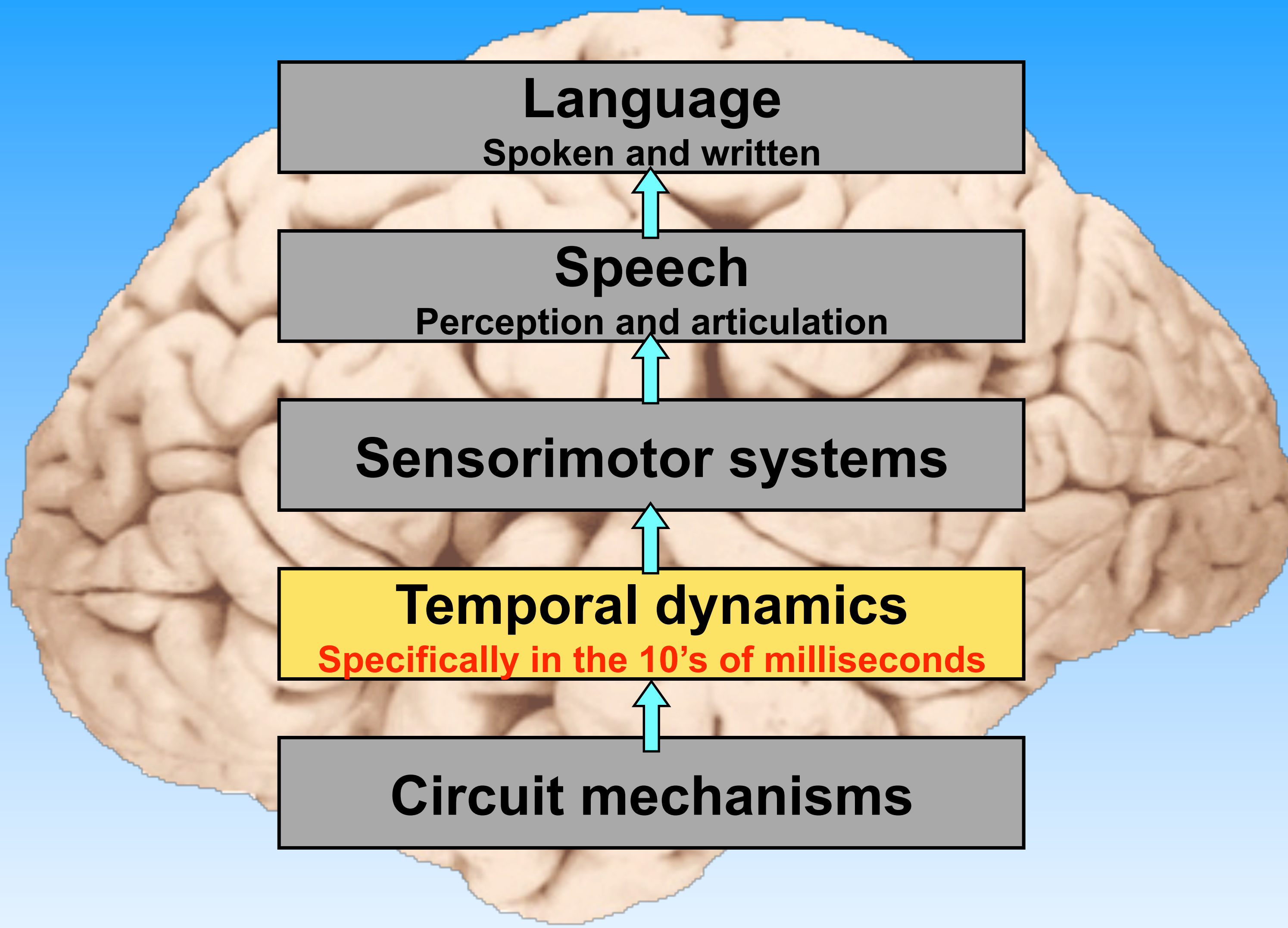


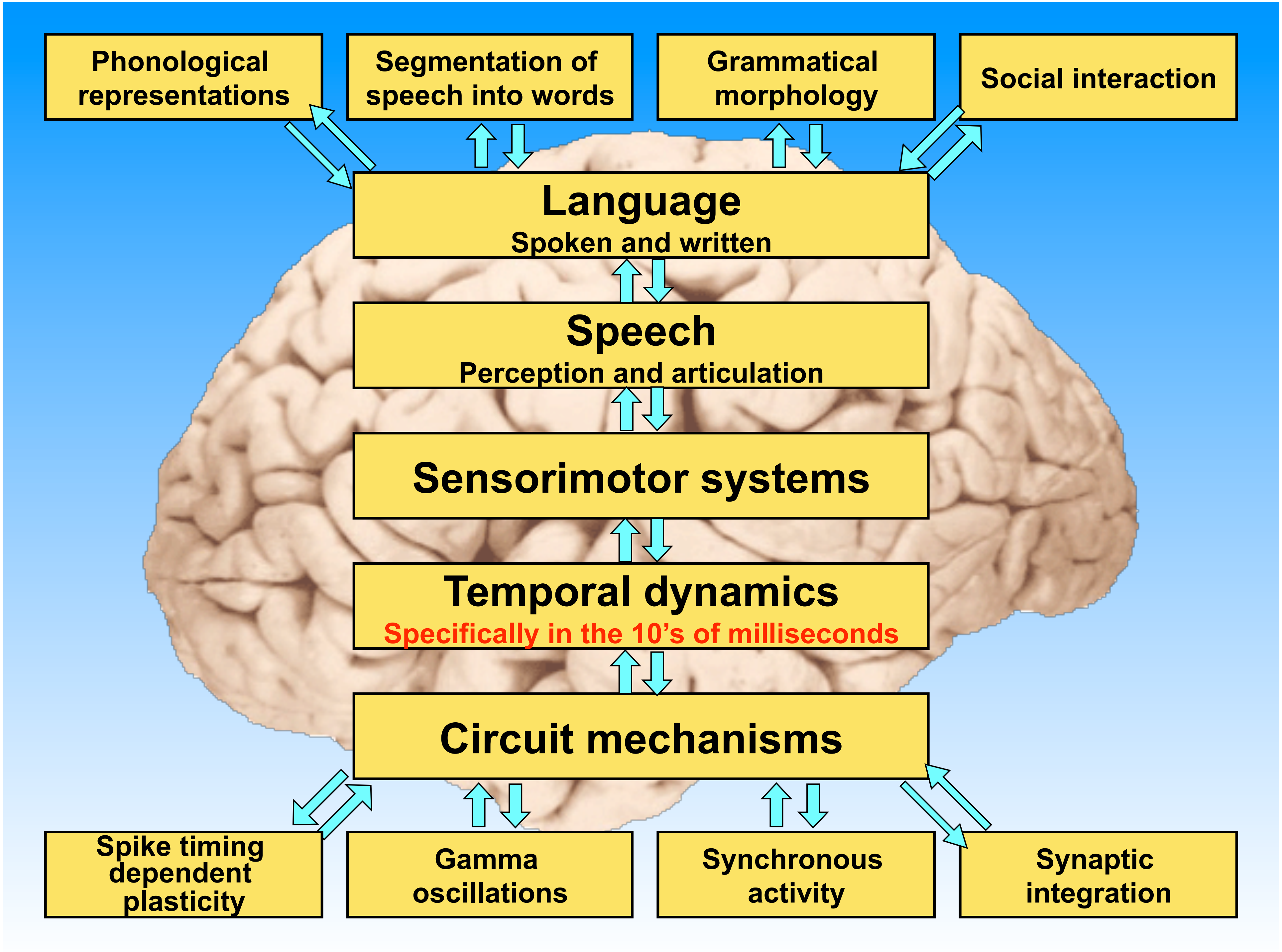
Specifically, thinking of speech from a sensorimotor systems perspective

Neurobiology of Language

A culmination of over 30 years of research with typically developing as well as language impaired children has led us to hypothesize an experience-dependent, developmental model in which **temporal dynamics** (specifically in the tens of millisecond time range) serves as the conduit between some of the most basic circuit level mechanisms and many of the fundamental components of language.

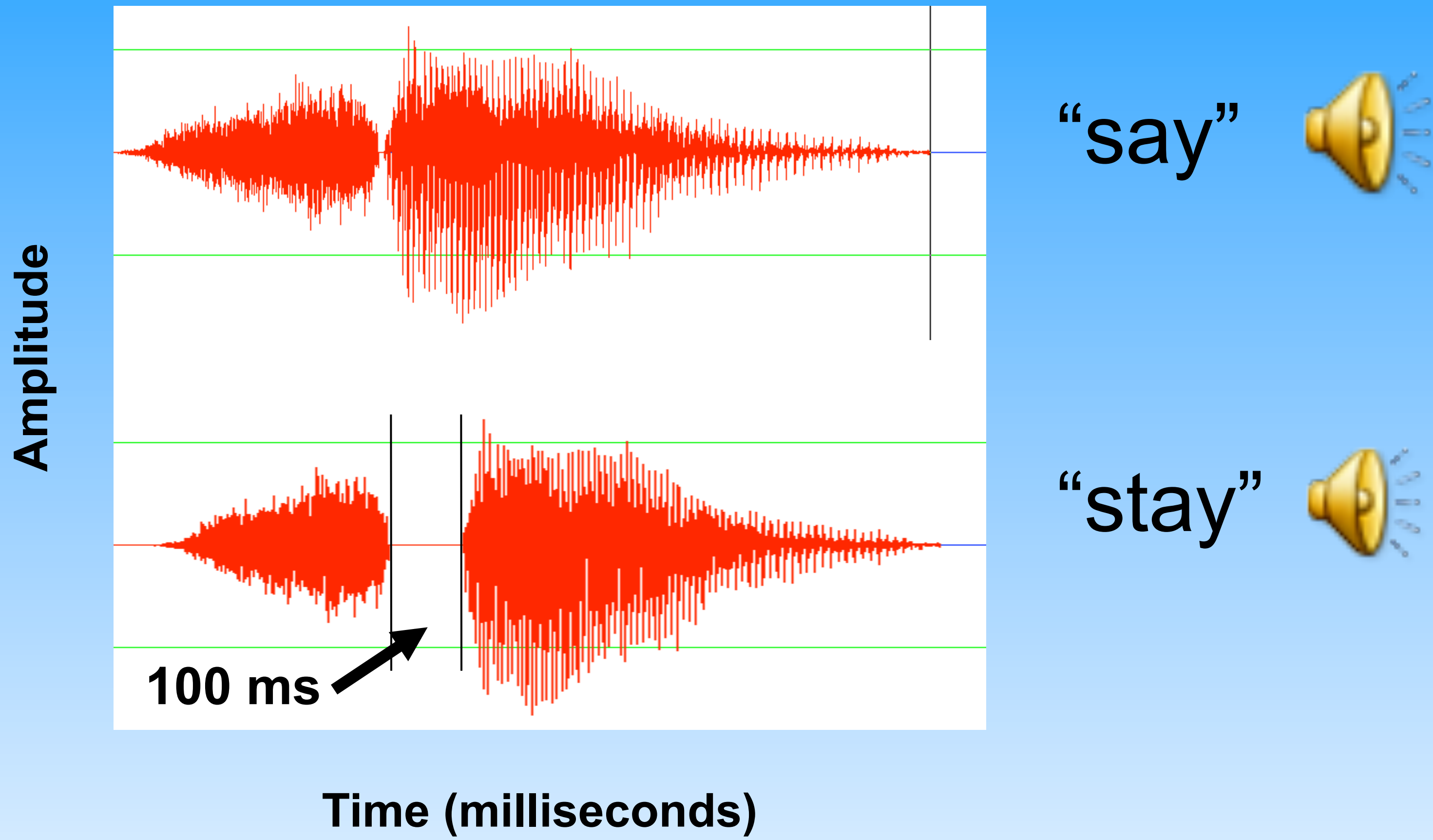
Neurobiology of Language





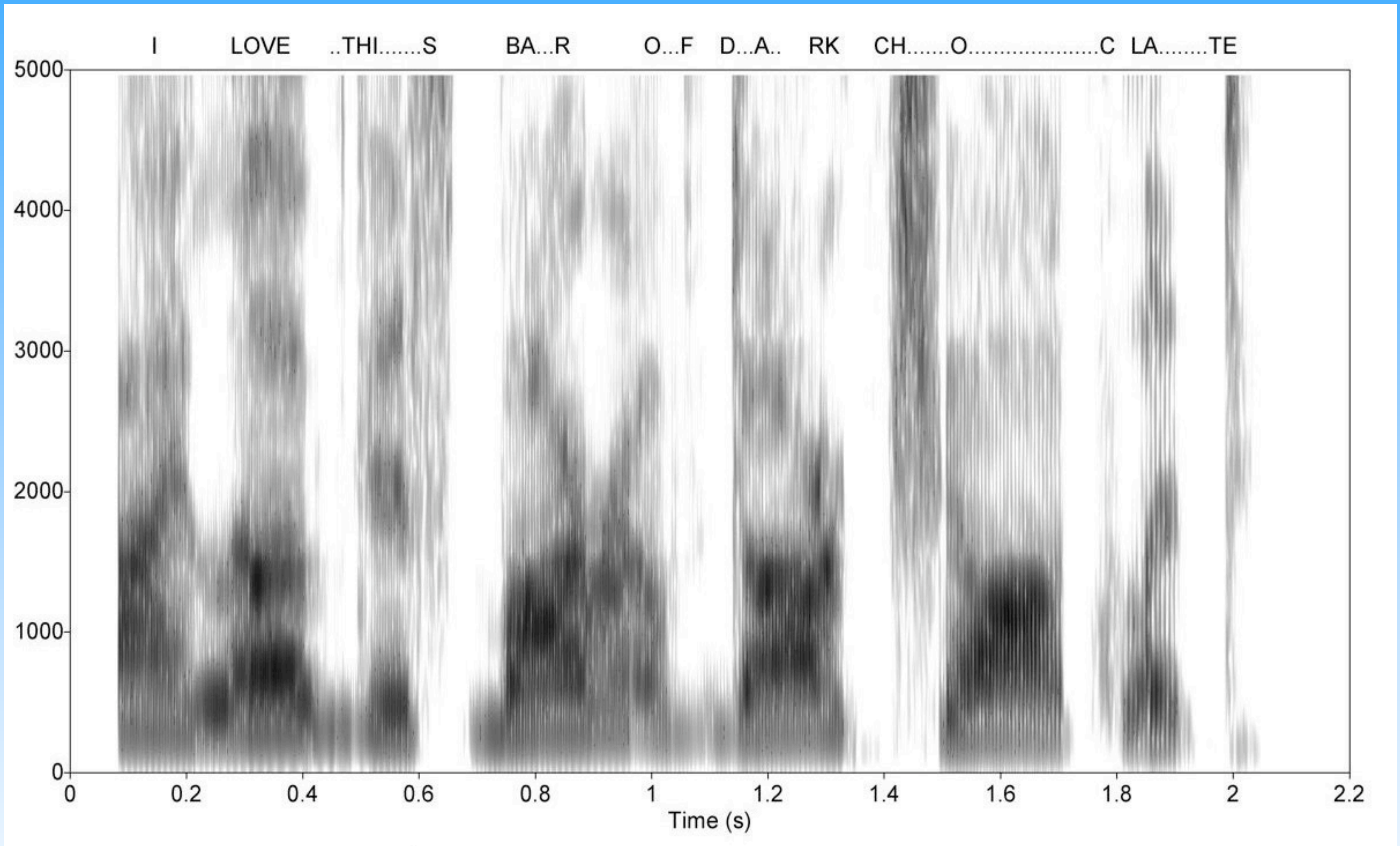
Phonological representations
Segmentation of speech into words
Grammatical morphology
Social interaction
Language
Spoken and written
Speech
Perception and articulation
Sensorimotor systems
Temporal dynamics
Specifically in the 10’s of milliseconds
Circuit mechanisms
Spike timing dependent plasticity
Gamma oscillations
Synchronous activity
Synaptic integration

For speech, 10's of milliseconds can change the meaning of a word



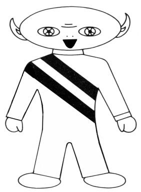
These waveforms are identical except for an inserted 100ms silent gap, yet we hear two different words. In order to be able to read and spell we need to hear these small acoustic differences in words.

Within the ongoing acoustic speech stream, words are not acoustically segmented



Speech stream exposure task

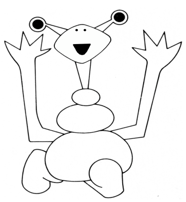
Unstressed Language:



nimoluvorifaliduranimoluliduravorifa

Transitional Probabilities Only

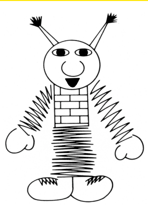
Stressed Language:



NImoluvorifa**LI**duranimoluliduraVOrifa

Transitional Probabilities + Prosodic Cues

Random Syllables:



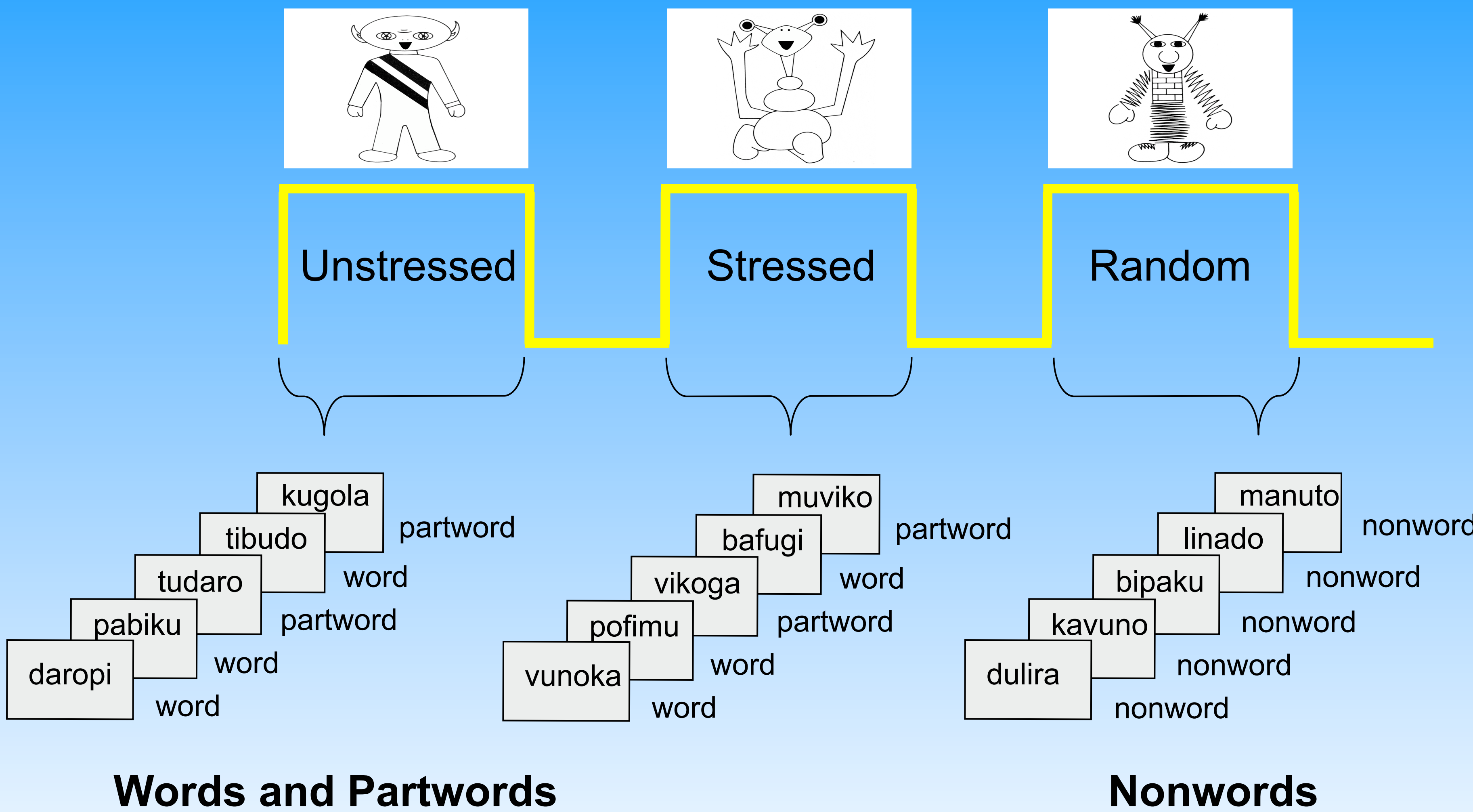
falidunuralifadulumorivoramamoninura

No Transitional Probabilities

No Prosodic Cues

Mc Nealy et al.,(2007) J. Neurosci. 26, 7629-7639

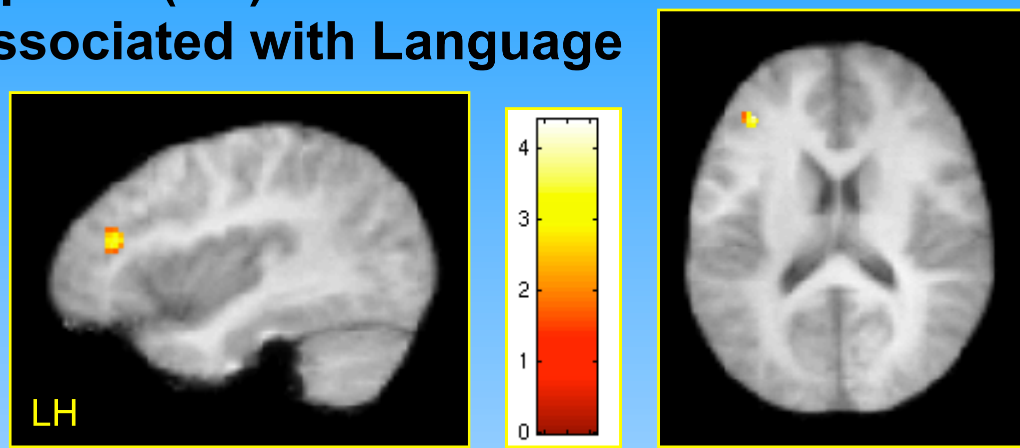
Word/partword discrimination task

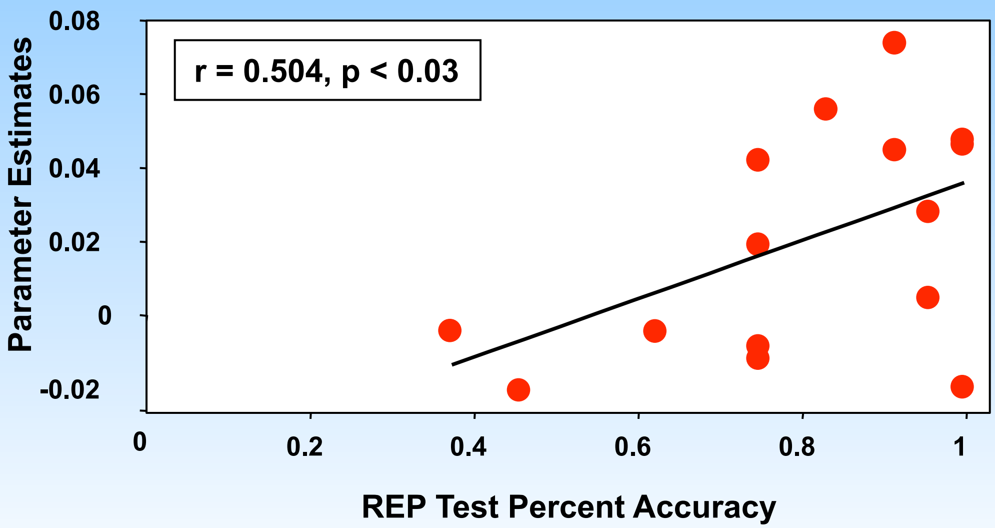


McNealy et al., (2006) J. Neurosci. 26, 7629-7639

fMRI Activity - Word > Nonword

Activates Left Hemisphere (LH) Frontal Areas Traditionally Associated with Language





Greater activity is correlated with better rapid auditory processing skills

McNealy et al.,(2006) J. Neurosci. 26, 7629-7639

The left hemisphere exhibits specialization for temporal dynamic processing

Temporal dynamic processing (specifically in the 10s of milliseconds) has been shown to activate left hemisphere-specific brain regions traditionally associated with language

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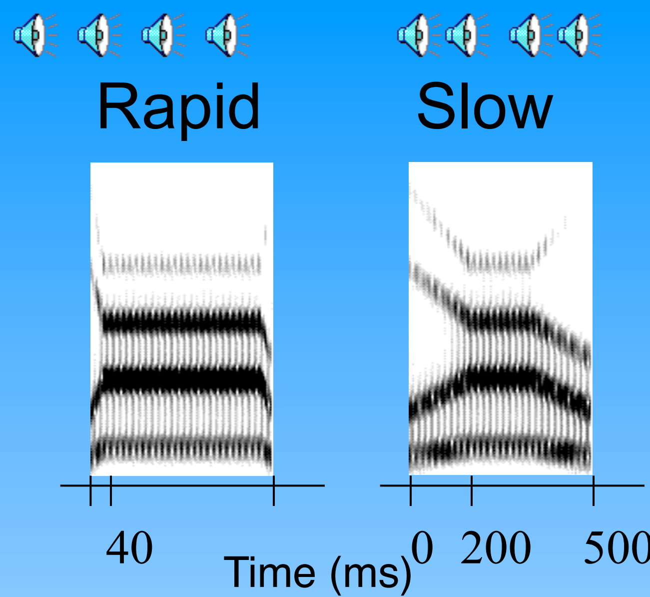
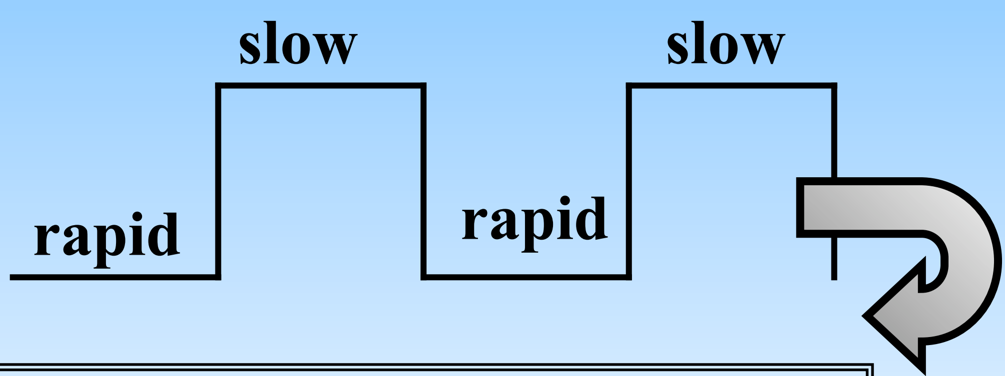
- Stimuli
  - Non-Speech Analogues
    - frequency transition
      - rapid & slow
    - ½ high pitch, ½ low pitch



- Task
  - push for high pitch
  - rapid, slow blocks



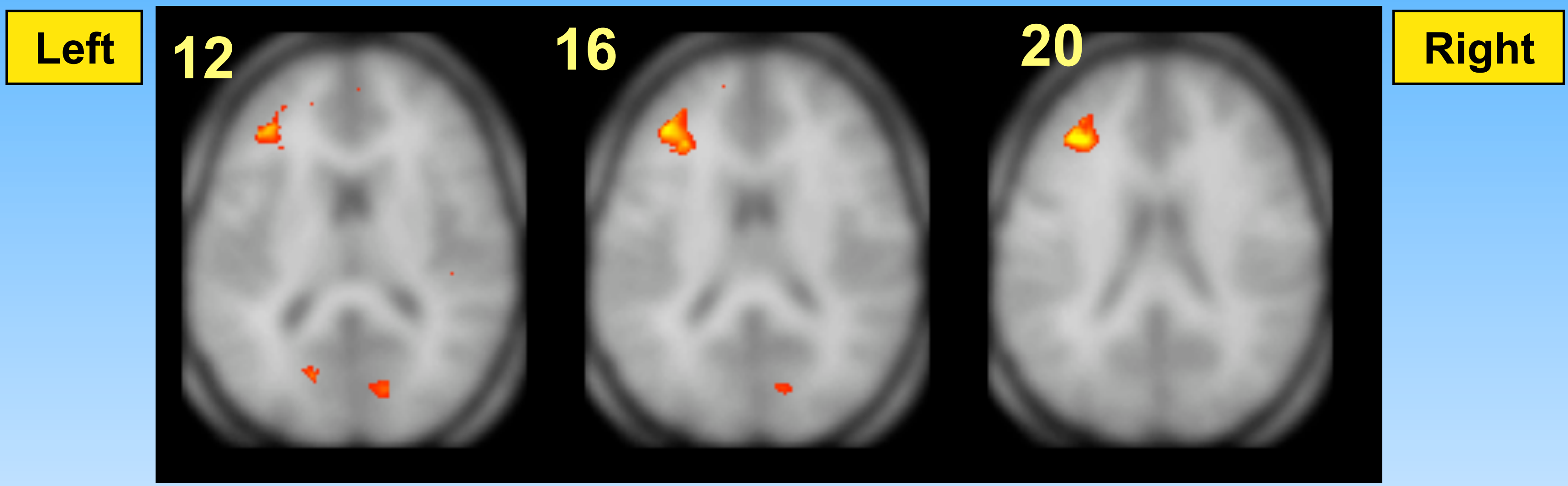
10 tones/ block, 6 blocks, Total time = 342 sec

Clustered volume acquisition

(Temple et al., 2000)

Left hemisphere-specific response to rapid non-speech analog spectrotemporal acoustic stimuli

fMRI Results: Fast > Slow



- **Left Middle Frontal Gyrus**
- **BA 46**

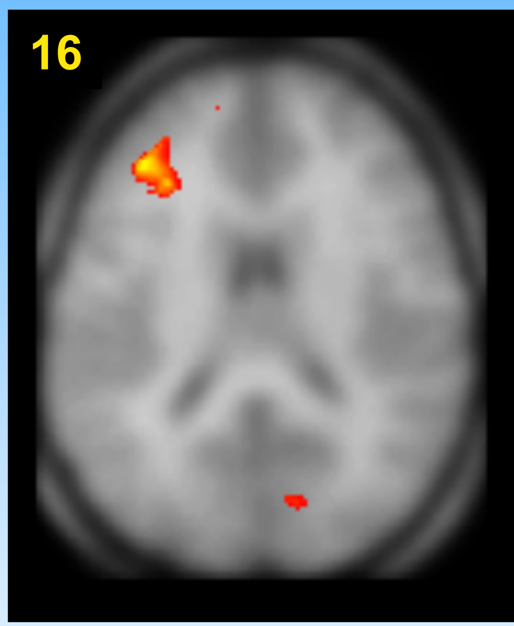
Temple et al. (2000) PNAS, 97.

Dyslexics fail to show left hemisphere-specific response to rapid non-speech spectrotemporal acoustic stimuli

fMRI Results: Fast > Slow

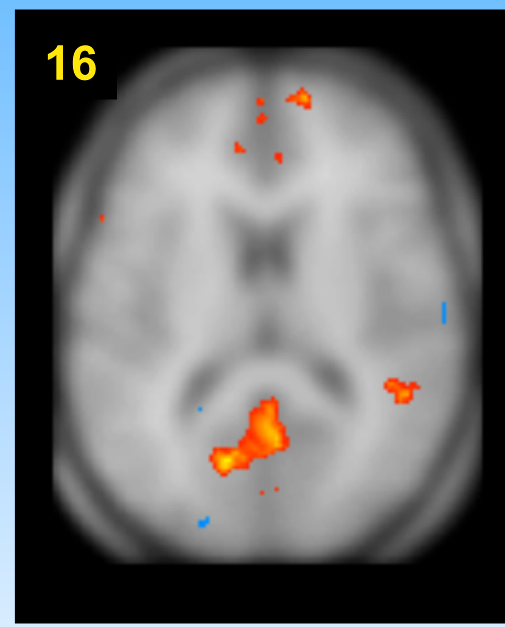
Control Group

Left



Frontal Regions
MFG (BA 46)

Dyslexic Group

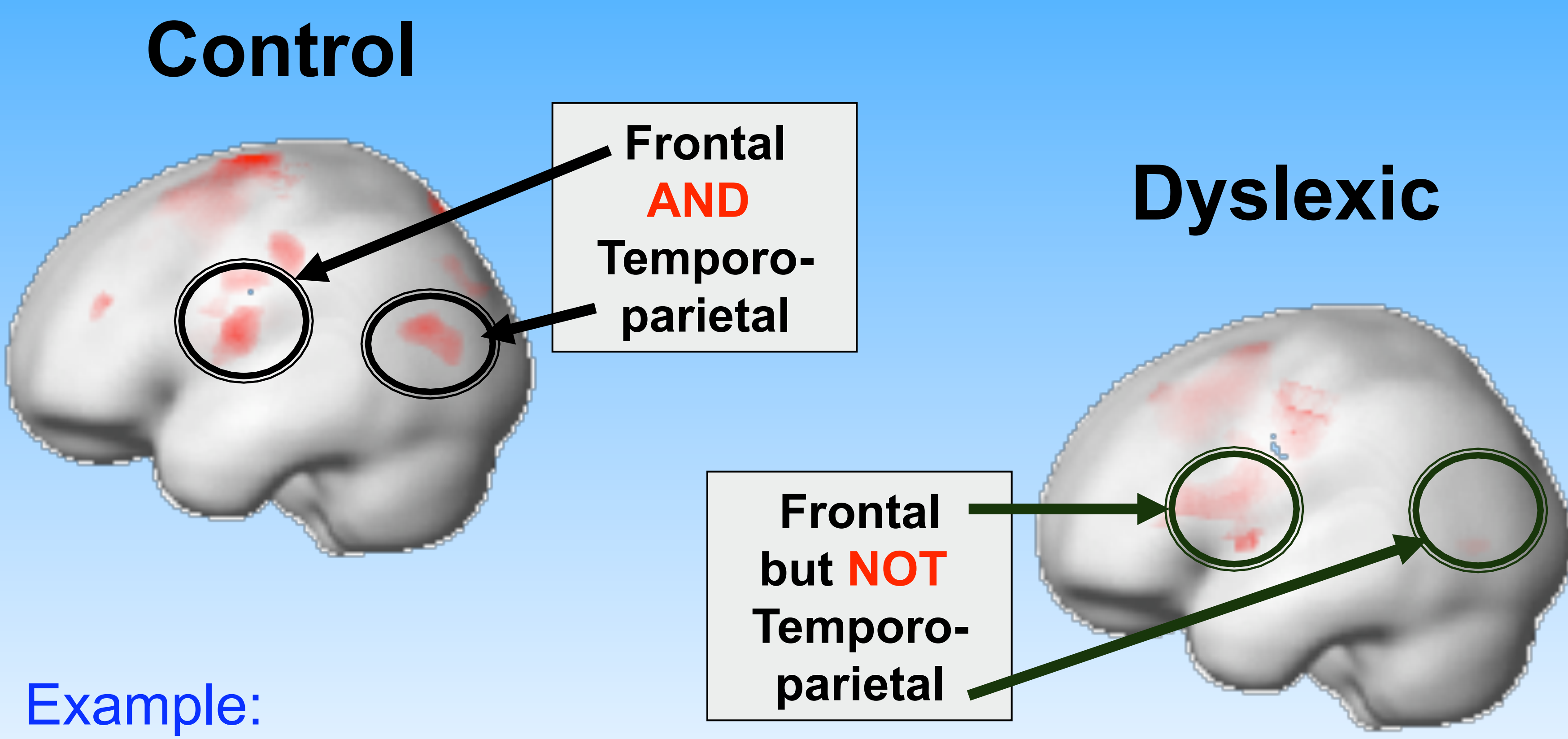


Right

No Activity

Temple et al. (2000) PNAS, 97.

fMRI activation while viewing two letters and determining whether their names rhyme



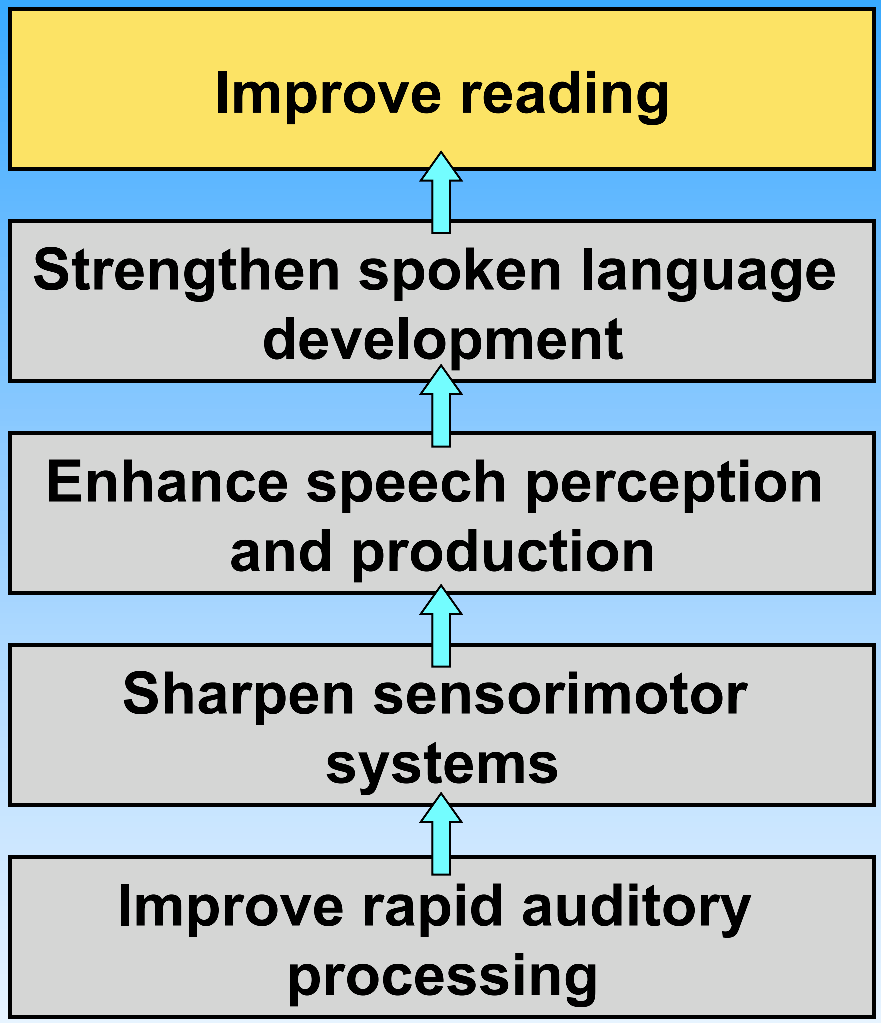
Example:

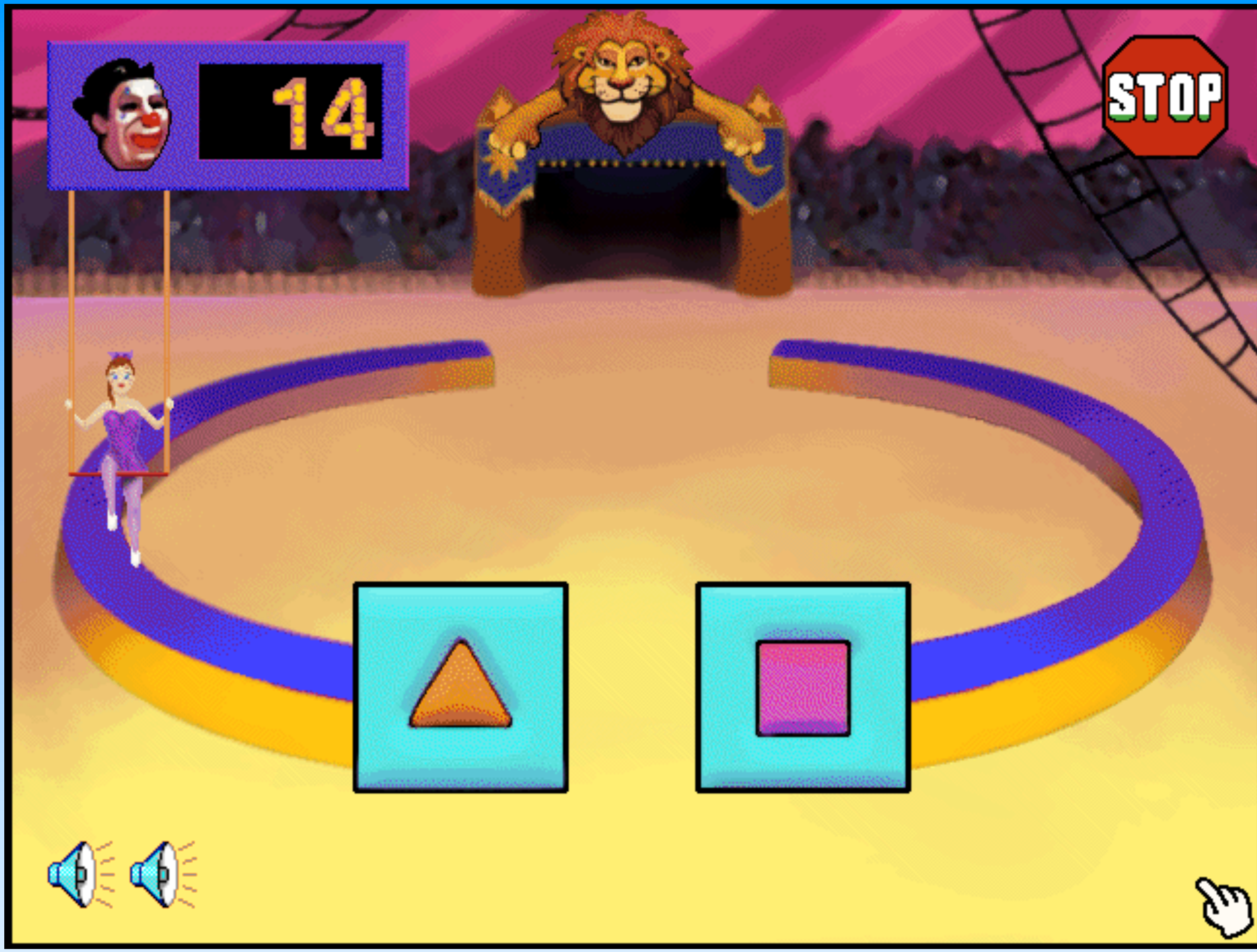
B D = Rhyme

B K = Do Not Rhyme

Temple et al. (2003) PNAS, 100.

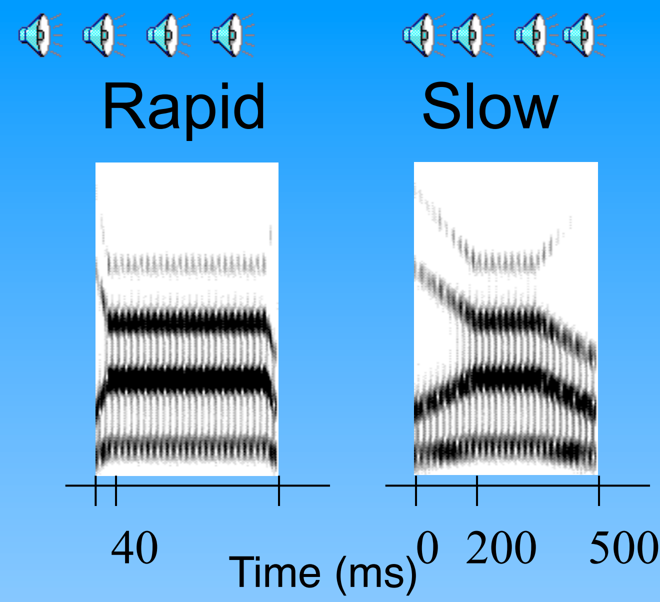
Goals for intervention



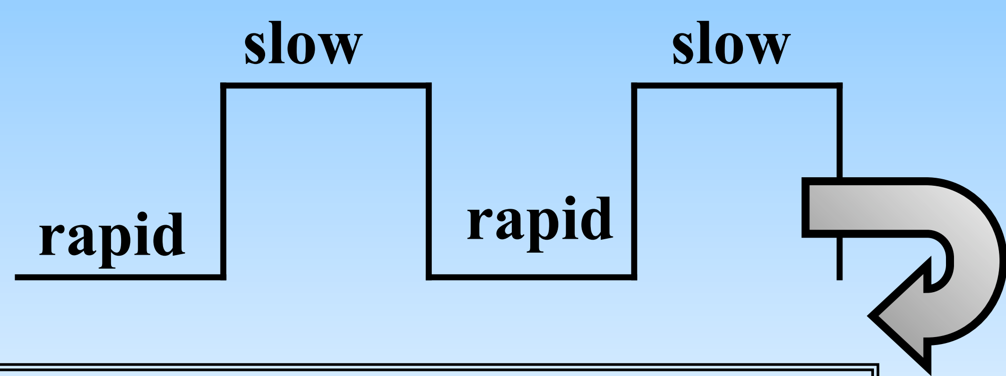


- The goal of this exercise is to detect whether the two tones are both rising, both falling, or rising and falling
- As training progresses the rate of presentation increases

- Stimuli
  - Non-Speech Analogues
    - frequency transition
      - rapid & slow
    - ½ high pitch, ½ low pitch



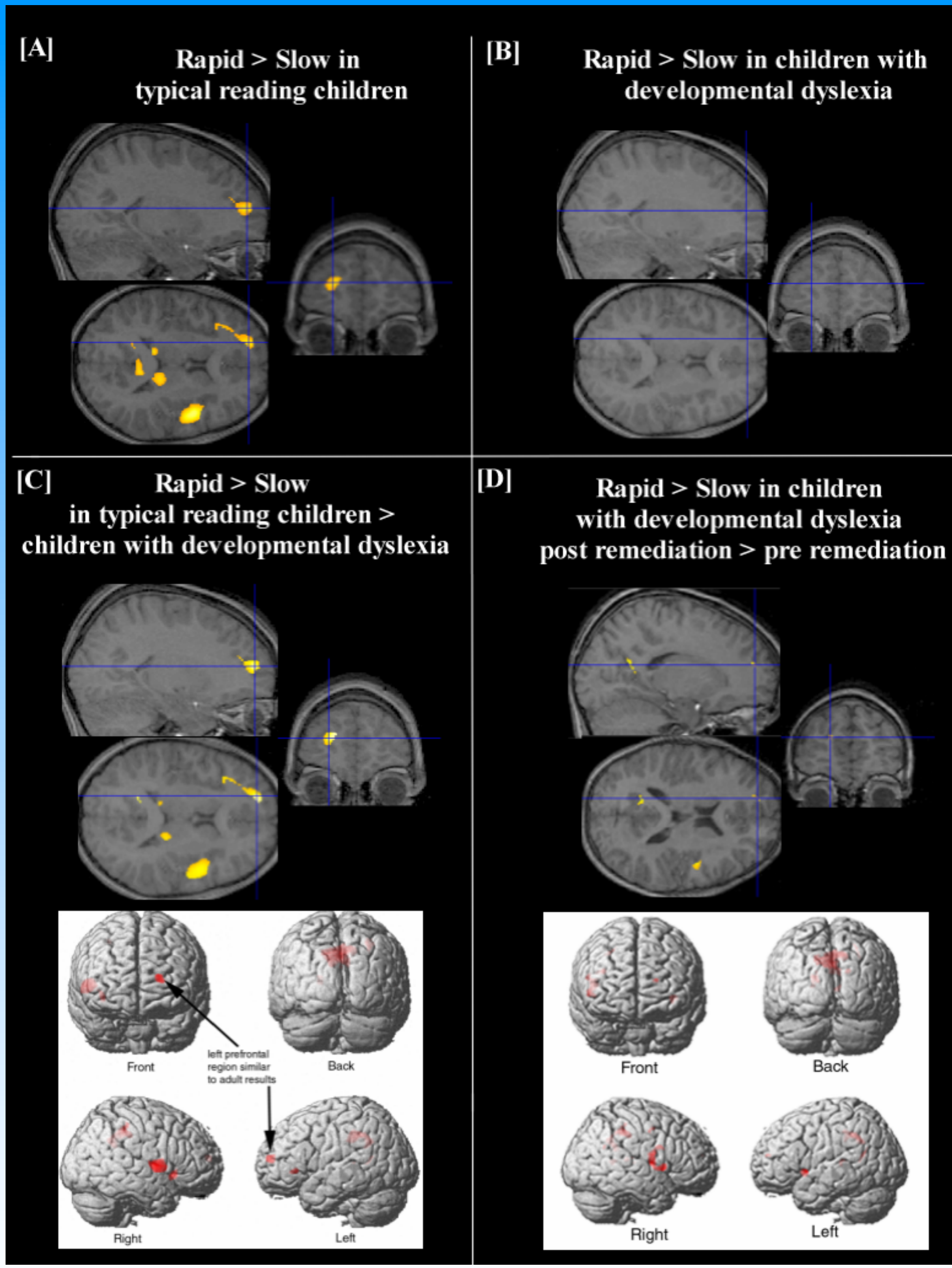
- Task
  - push for high pitch
  - rapid, slow blocks



10 tones/ block, 6 blocks, Total time = 342 sec

Clustered volume acquisition

Training paradigm!
(Fast ForWord ®)



- This study is the first to reveal a network of brain areas sensitive to the rapidity of non-linguistic auditory stimuli in typical-reading children, and a disrupted response in children with developmental dyslexia.

- Area B10 in adults:
  Belin et al., 1998; Temple, 2000 (identical stimuli)
  Poldrack et al. (2001) (compressed sentences)

- Additionally, this disrupted response was partially ameliorated through remediation that improved language and reading ability in children with developmental dyslexia.

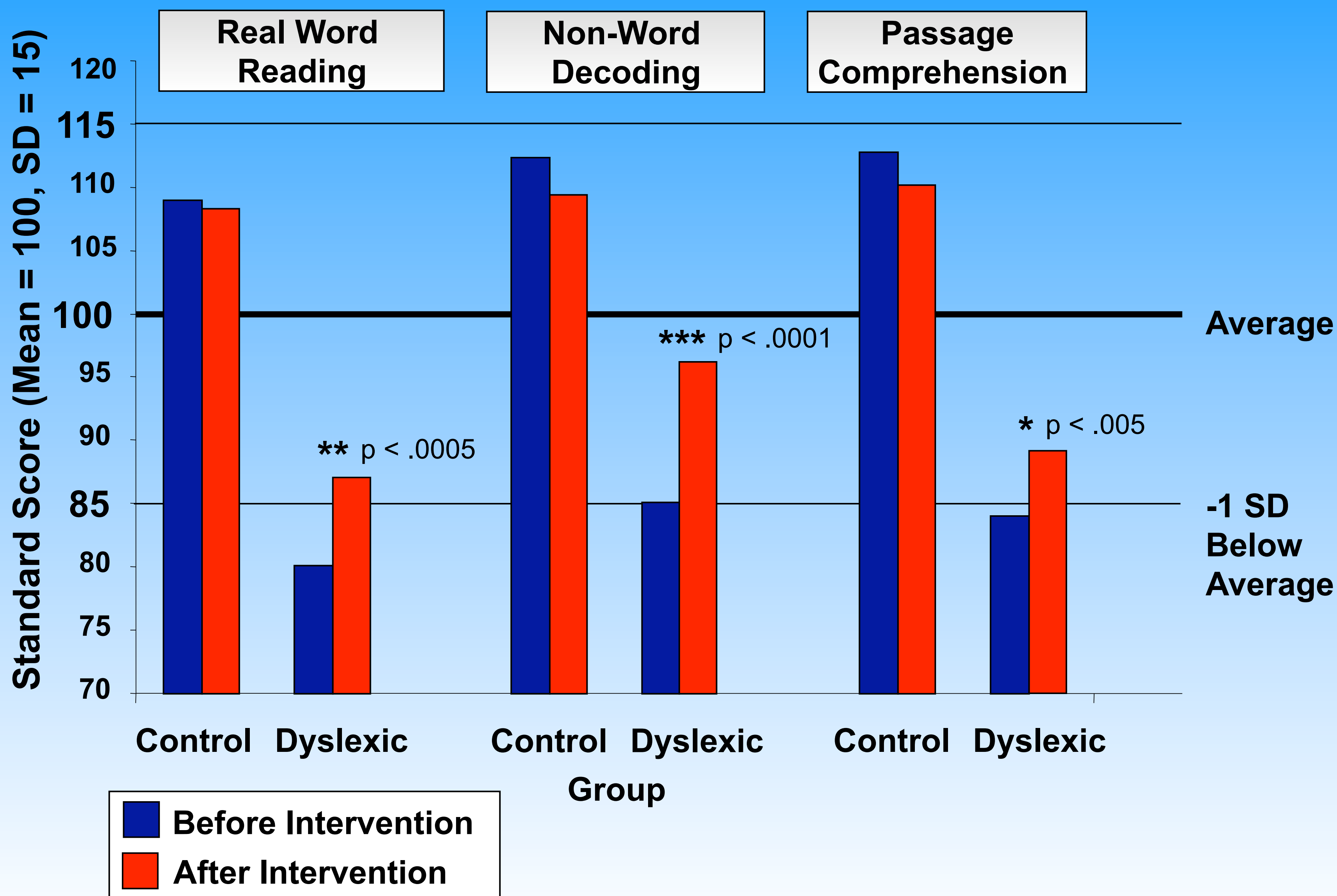
Gaab et al., (2007) Rest. Neurol.Neuro. 25, 295-310

Behavioral improvement:

	Children with Developmental Dyslexia			Typical-Reading Children		
	Before remediation	After remediation	Sig.	1st scan (n=12)	2nd scan (n=12)	Sig.
Subjects	22 (6 F))	22 (6 F))	----	12 (3F)	12 (3 F)	----
Word reading (WJRMT-R ID)	77.4 (9.7)	87.0 (6.9)	p<0.0001	108.8 (6.7)	107.7 (8.1)	p>0.1
Non-word decoding (WJRMT-R WA)	86.2 (6.1)	95.5 (7.3)	p<0.00005	110.6 (8.7)	108.7 (8.3)	p>0.1
Written Comprehension (WJRMT-R PC)	85.6 (10.3)	89.7 (8.2)	p<0.005	112.8 (4.5)	109.6 (6.5)	p<0.03
Listening comprehension (WJ-R LC)	109.5 (15.2) (n=21)*	118.6 (16.4) (n=21)*	p<0.005	120.1 (11.6)	121.3 (10.9)	p>0.1
Receptive language (CELF-3 REC)	94.5 (12.3)	103 (14.5)	p<.005	118.9 (7.9)	124. 1 (9.7)	p=0.08
Expressive language (CELF-3 EXP)	95.0 (14.4)	102.7 (16.9)	p<0.005	111.9 (8.8)	114.4 (12.5)	p>0.1
Total language (CELF-3 TOT)	94.0 (14.1)	102.5 (15.4)	p<0.0005	115.8 (8.4)	119.8 (10.3)	p>0.1
Phonological awareness (CTOPP PA)	94.2 (8.4) (n=18)*	101.2 (13.3) (n=18)*	p<0.01	103.25 (9.3)	107 (11.2)	p=0.06
Phonological memory (CTOPP PM)	93.3 (13.15) (n=18)*	100.8 (15.2) (n=18)*	p<0.005	100.3 (10.3)	102.8 (12.5)	p>0.1
Rapid naming (CTOPP RN)	81.8 (9.5) (n=18)*	86.4 (10.6) (n=18)*	p<0.005	106 (6.8)	104 (11.5)	p>0.1

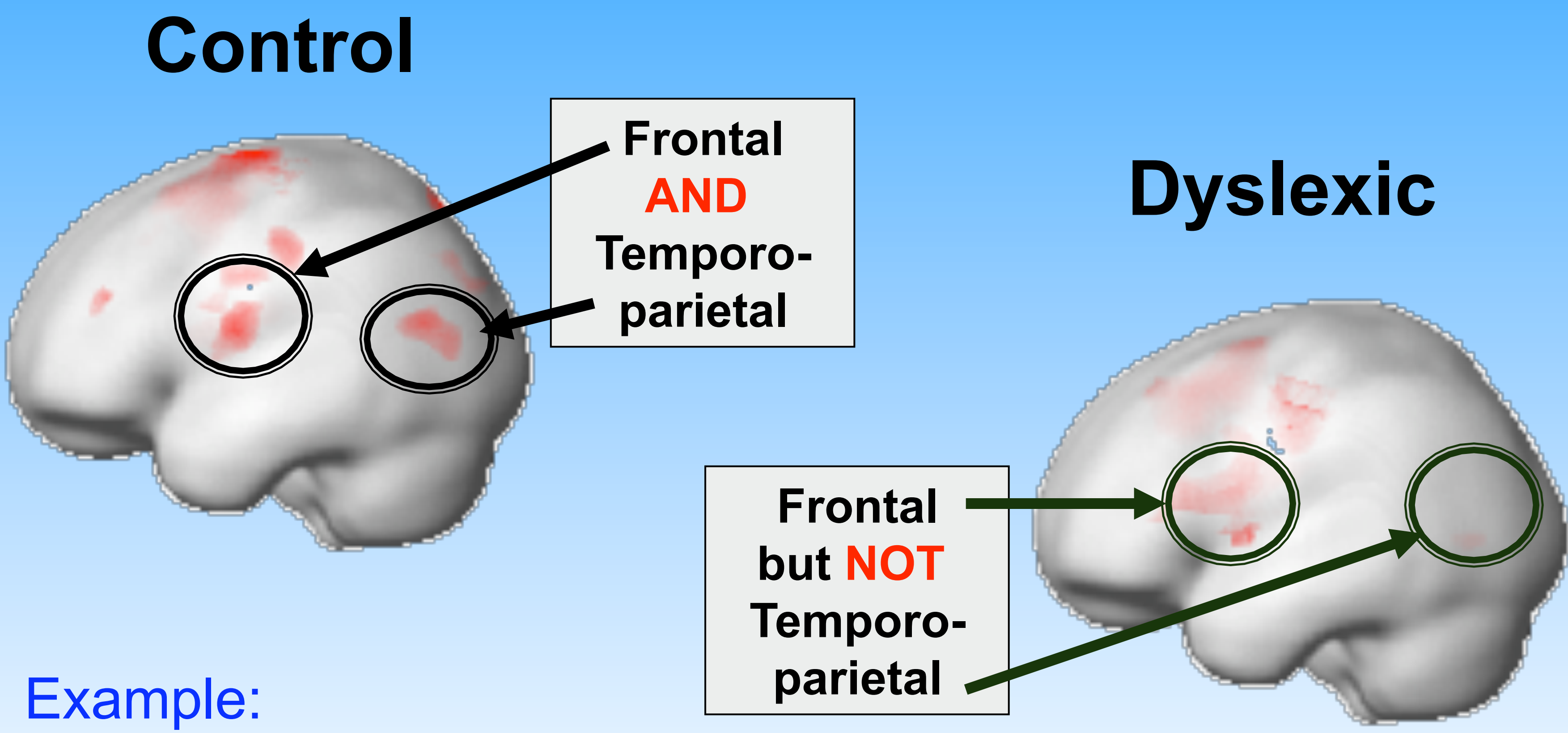
No differences between DD (after remediation) and TR (2nd test)

Reading improvements after intervention



Temple et al. (2003) PNAS 100.

fMRI activation while viewing two letters and determining whether their names rhyme



Example:

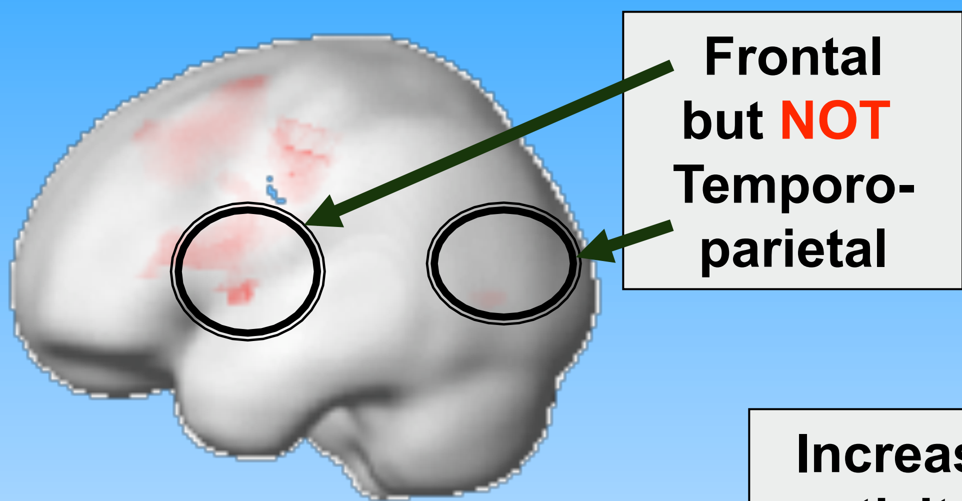
B D = Rhyme

B K = Do Not Rhyme

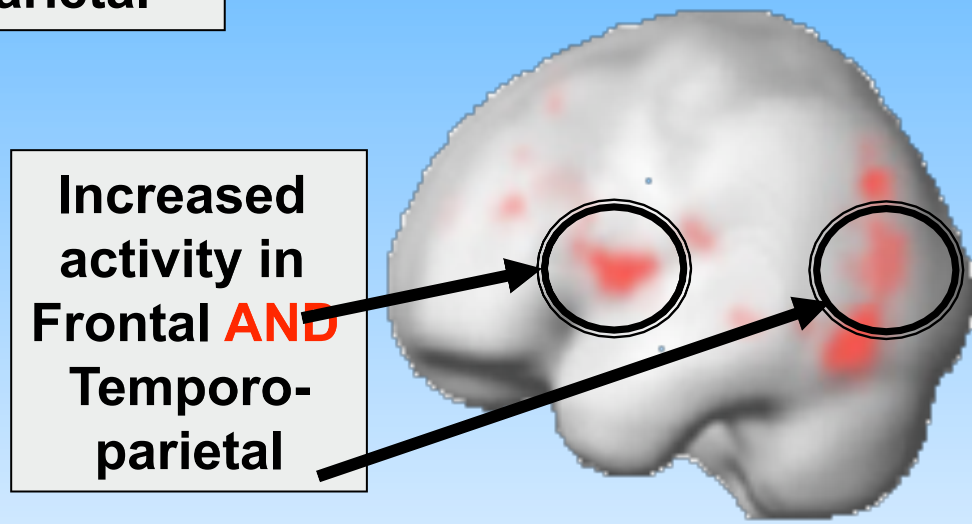
Temple et al. (2003) PNAS, 100.

Neural effects of intervention in dyslexic children

Pre-Intervention



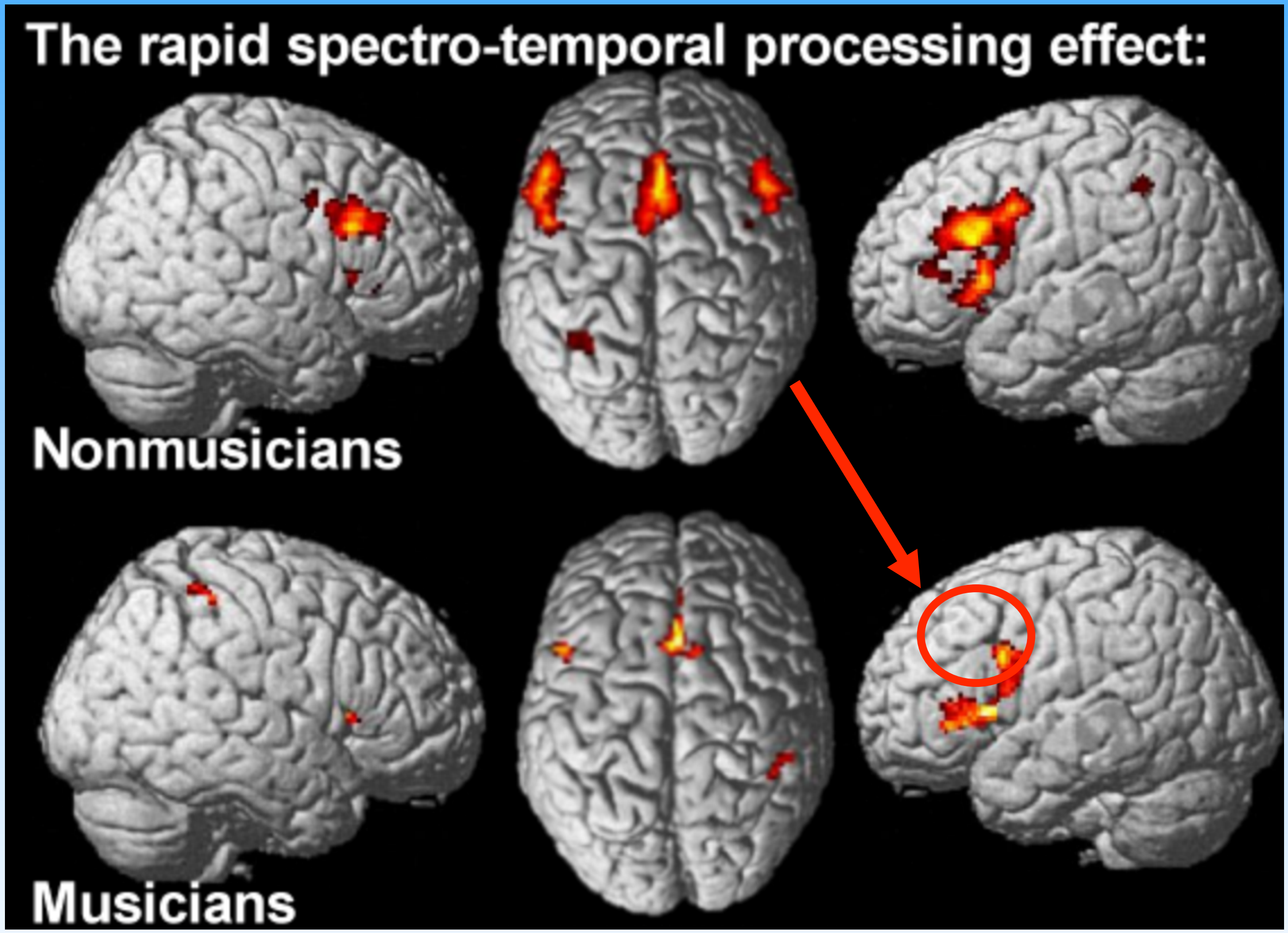
Post-Intervention



After training, metabolic brain activity in dyslexics more closely resembles that of normal readers.

Temple et al. (2003) PNAS, 100.

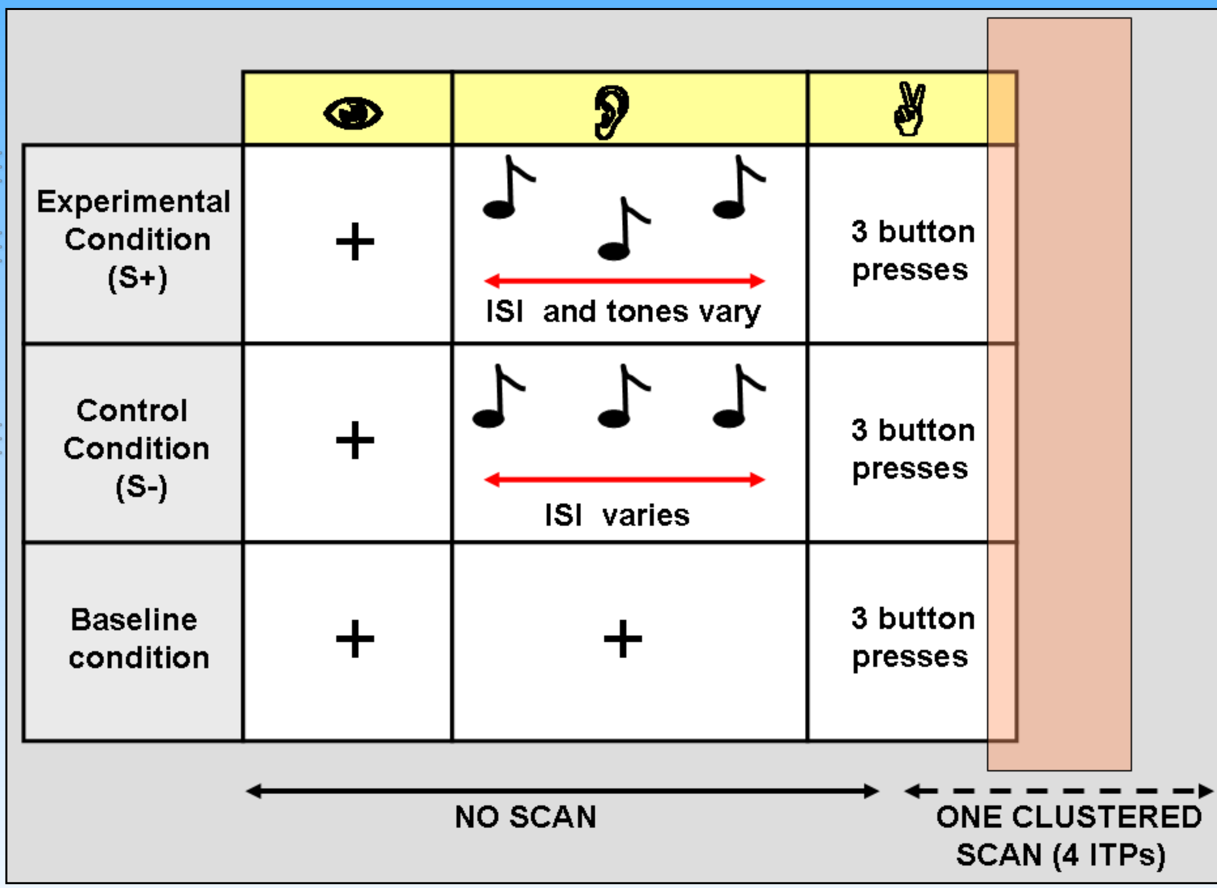
Musical training alters the **functional anatomy** of **rapid spectro-temporal processing** resulting in **improved behavioral performance** along with a more **efficient** network primarily involving **traditional language regions.**



Gaab et al.(2006)

Neural correlates of rapid spectro-temporal processing in musicians and nonmusicians

- 40 subjects (20 musicians/20 non-musicians)



- **2 complex tones (100/300Hz)**
- **Sequencing vs. Non-Sequencing**
- **ISIs: 5/20/50/300ms**
- **jittered sparse temporal sampling (Gaab et al. 2003, Gaab et al., in press a,b)**

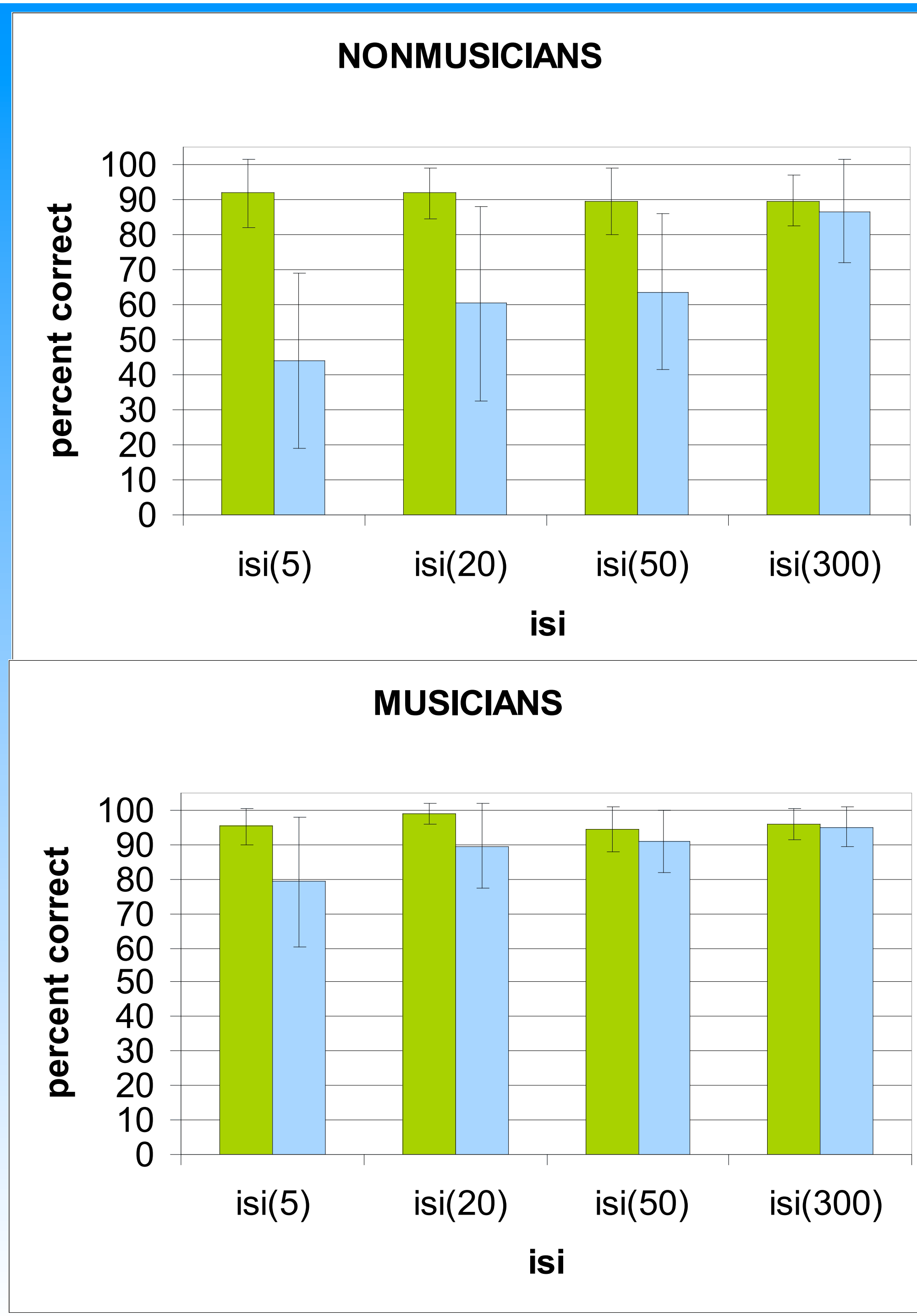
(Gaab et al. Ann. N.Y. Acad. Sci: 2006)

- Behavioral results:

ANOVA:
musicianship x ISI x condition

Main effect: condition
Main effect: ISI
Main effect: musicianship
Interaction:
musicianship x ISI x condition

Sequencing
Non-sequencing



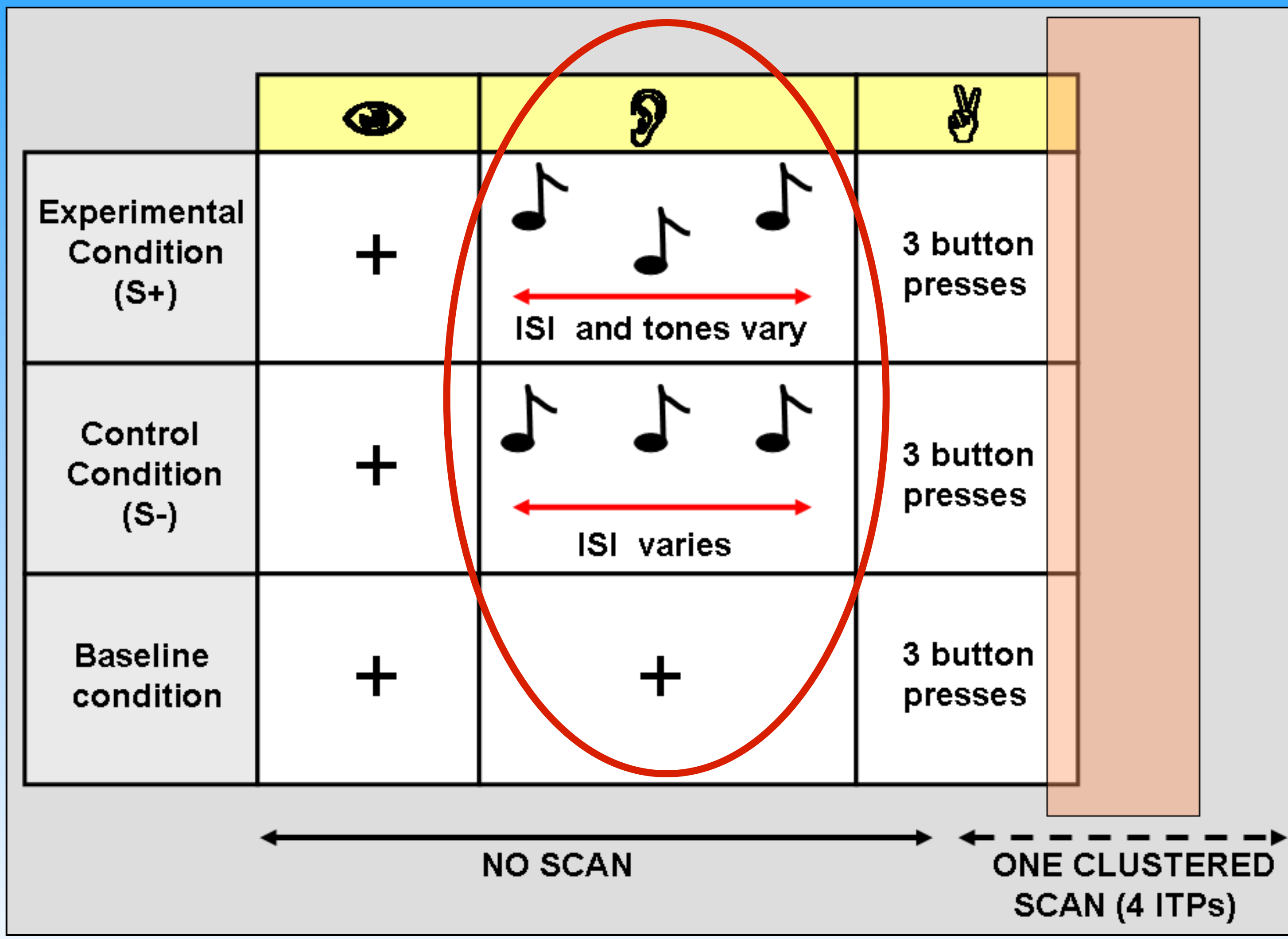
- Correlations for musician group:

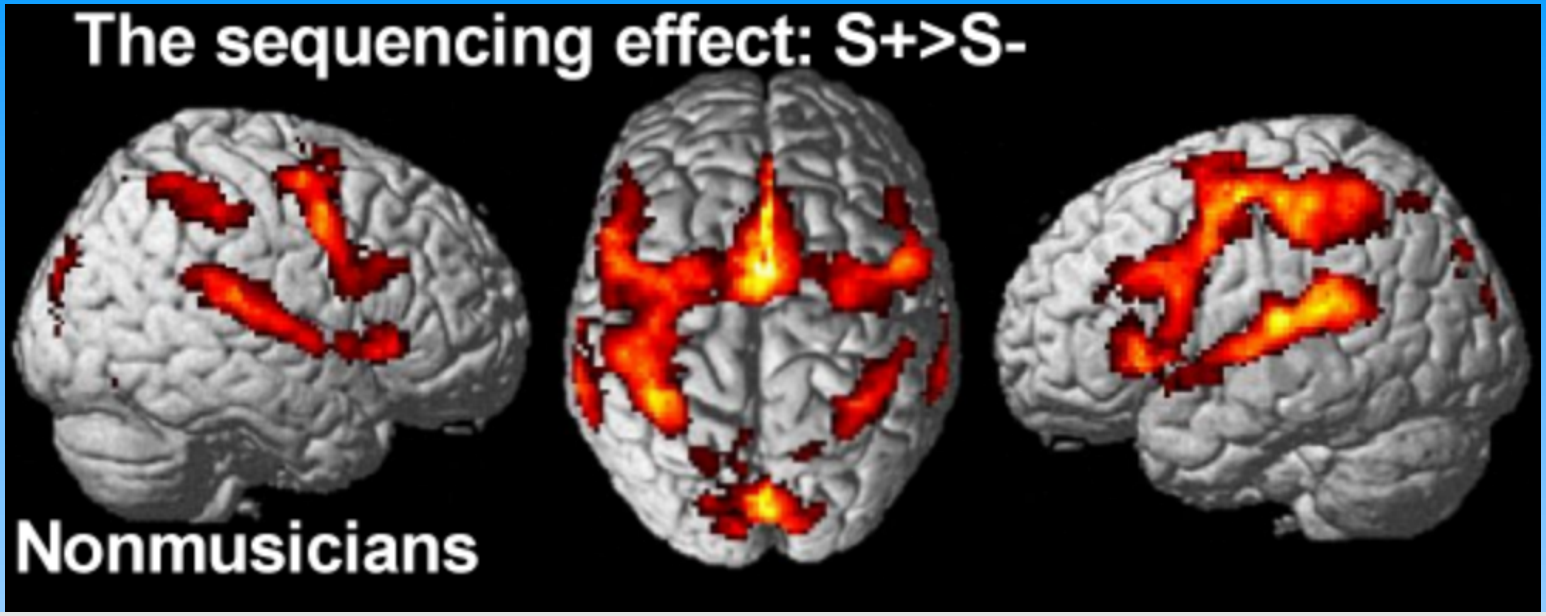
	Years played	Hrs. played last 2 years	Hrs. played last 5 years
Exp all (%corr)	0.50	0.40	0.45
Con all (%corr)	0.41	0.21	0.27
RT overall	-0.54	-0.26	-0.32
Exp1(%corr)	0.52	0.44	0.48
Con1(%corr)	0.18	0.15	0.19
Exp4(%corr)	0.24	0.22	0.24

p<0.01

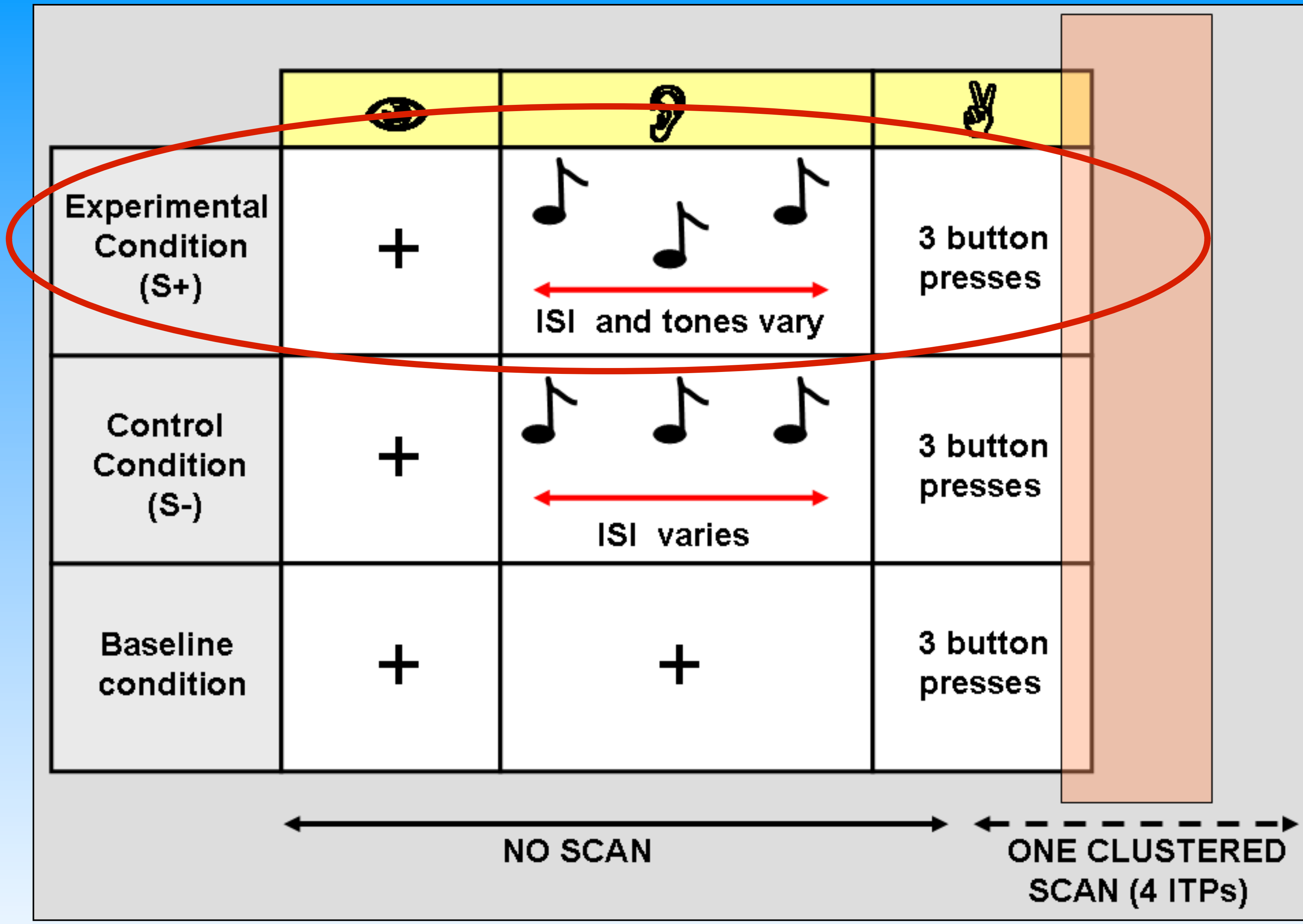
p<0.05

The sequencing effect:



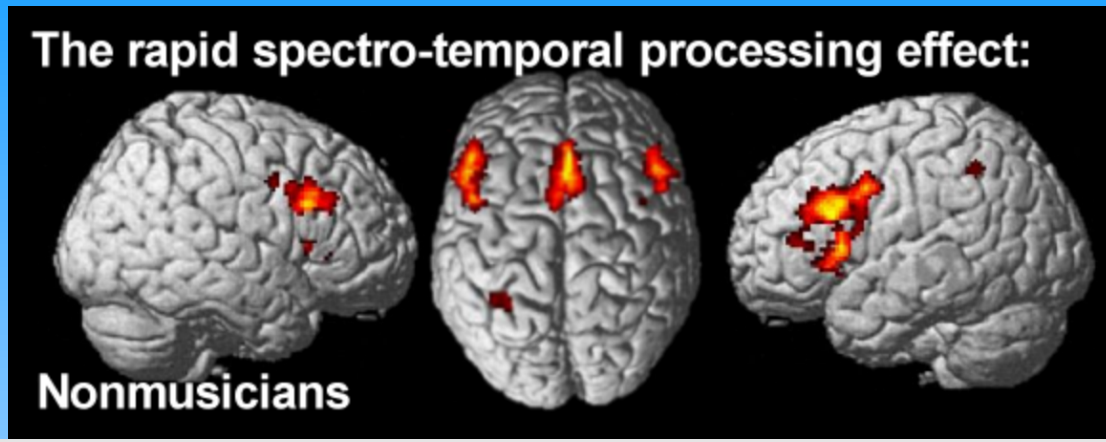


p<0.05 corrected

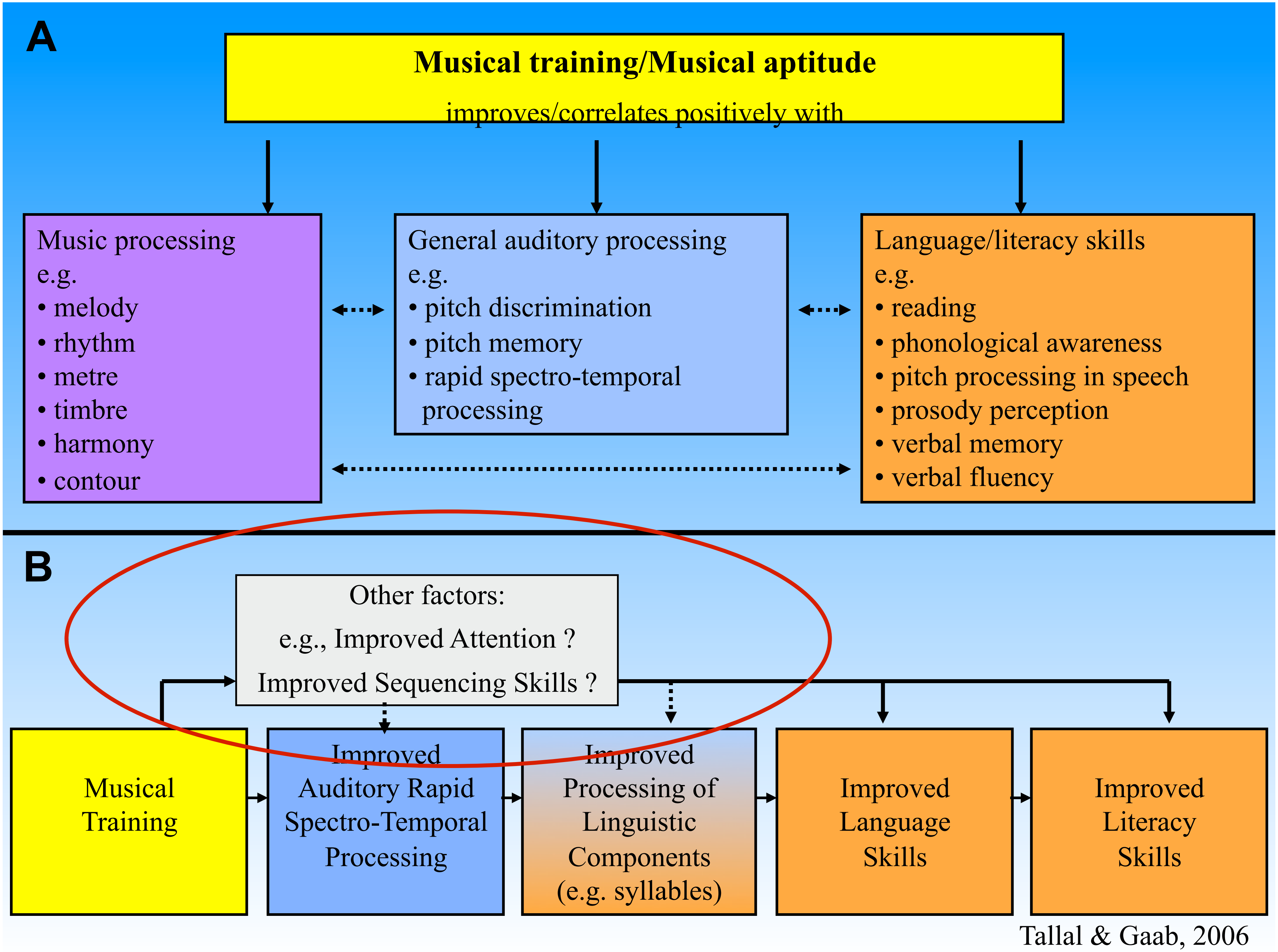


Experimental Condition (S+)
+
ISI and tones vary
3 button presses
Control Condition (S-)
+
ISI varies
3 button presses
Baseline condition
+
+
3 button presses
NO SCAN
ONE CLUSTERED SCAN (4 ITPs)

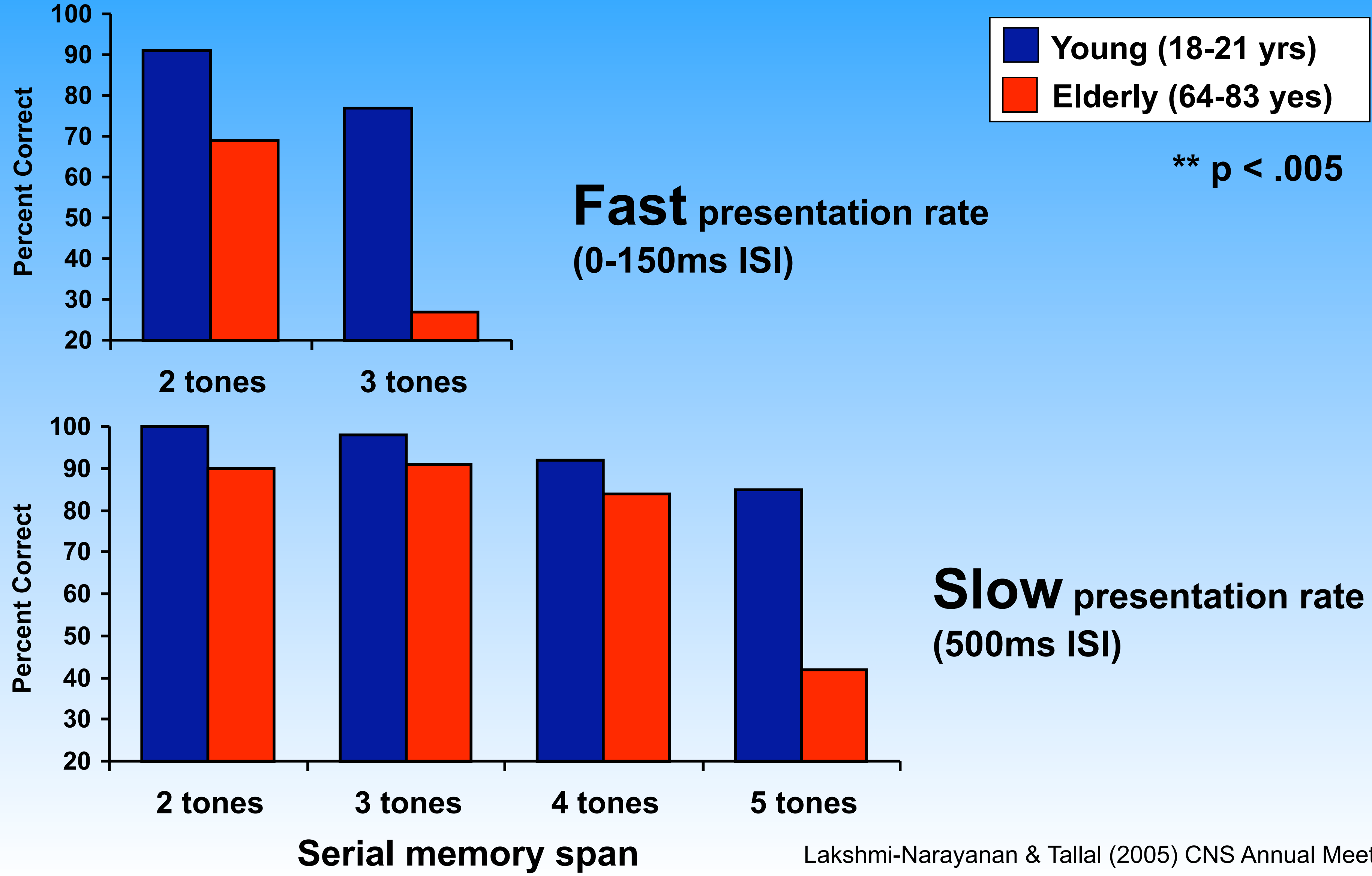
- The parametric analysis:



$p<0.05$ corrected


A
Musical training/Musical aptitude
improves/correlates positively with
Music processing
e.g.
• melody
• rhythm
• metre
• timbre
• harmony
• contour
General auditory processing
e.g.
• pitch discrimination
• pitch memory
• rapid spectro-temporal processing
Language/literacy skills
e.g.
• reading
• phonological awareness
• pitch processing in speech
• prosody perception
• verbal memory
• verbal fluency
B
Other factors:
e.g., Improved Attention ?
Improved Sequencing Skills ?
Musical Training
Improved Auditory Rapid Spectro-Temporal Processing
Improved Processing of Linguistic Components (e.g. syllables)
Improved Language Skills
Improved Literacy Skills
Tallal & Gaab, 2006

Memory problems in the elderly are exacerbated by their slower processing speed

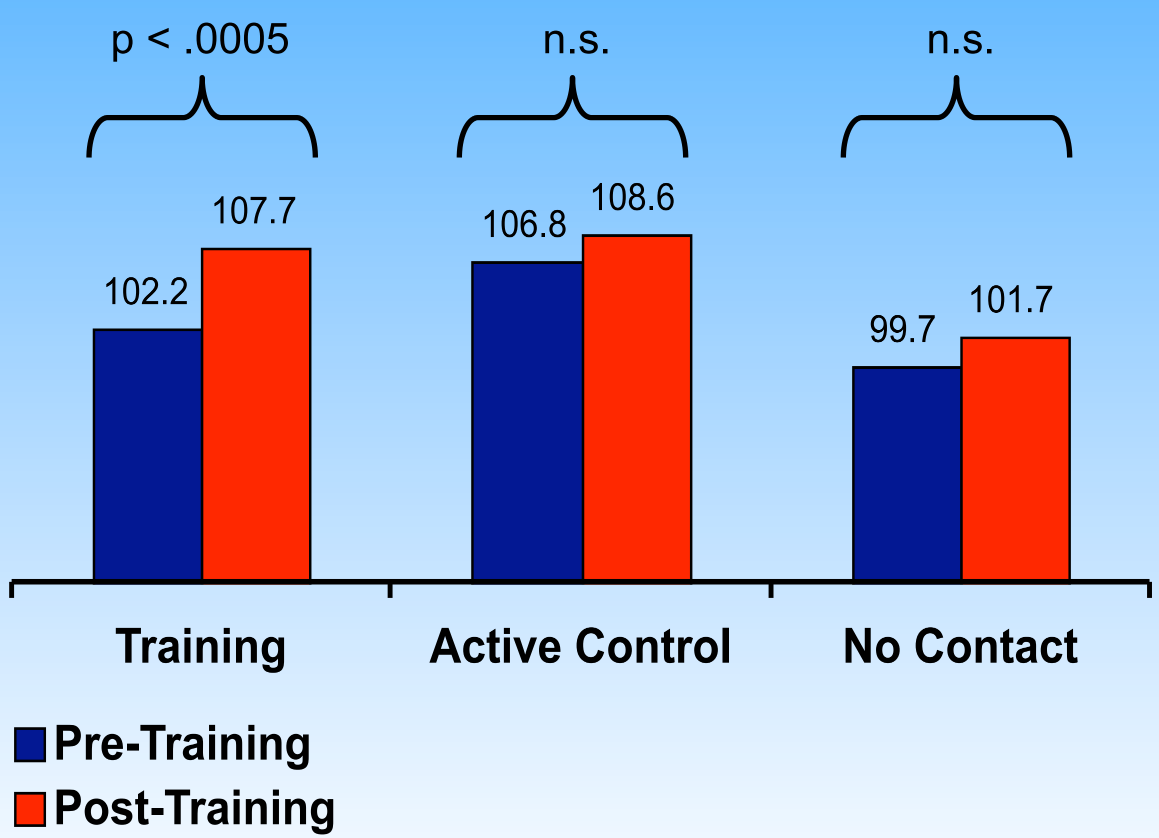


Lakshmi-Narayanan & Tallal (2005) CNS Annual Meeting

A brain plasticity based listening training program significantly enhanced memory in elderly adults

Overall neuropsychological function pre- and post-training

Age-normed scores



- Results from a pilot randomized controlled trial with 95 participants aged 64-95
- Intensive 8-week listening training program
- Memory improvement in training group is equivalent to ~10 years

See Hardy et al. (2005) SFN Poster # **408.7** Monday