Auditory Function in Patients with Parkinson Disease

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VA RR&D
NCRAR

Topics

- Previous studies of auditory function in this population
- Description of our study at NCRAR
- Findings from the study
- Recommendations

Parkinson Disease (PD)

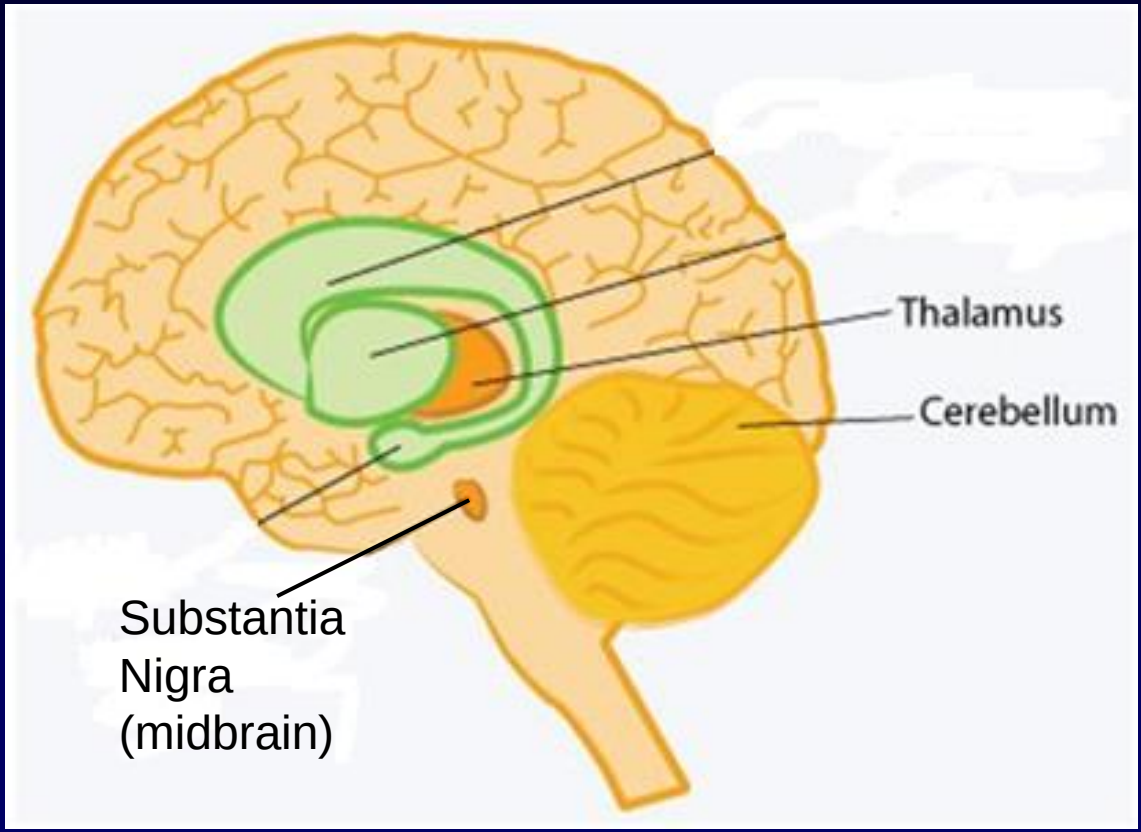
- Affects at least **one million** people in the U.S.
- PD is the second most prevalent neurodegenerative disorder (after Alzheimer's)
- Average age of diagnosis: **60 years**
- Signs/symptoms (**motor**):
    - Tremor (present in 70% of cases at onset)
    - Slowness of movement (bradykinesia), including planning and execution
    - Rigidity, stiffness, increased muscle tone
    - Postural instability – impaired balance

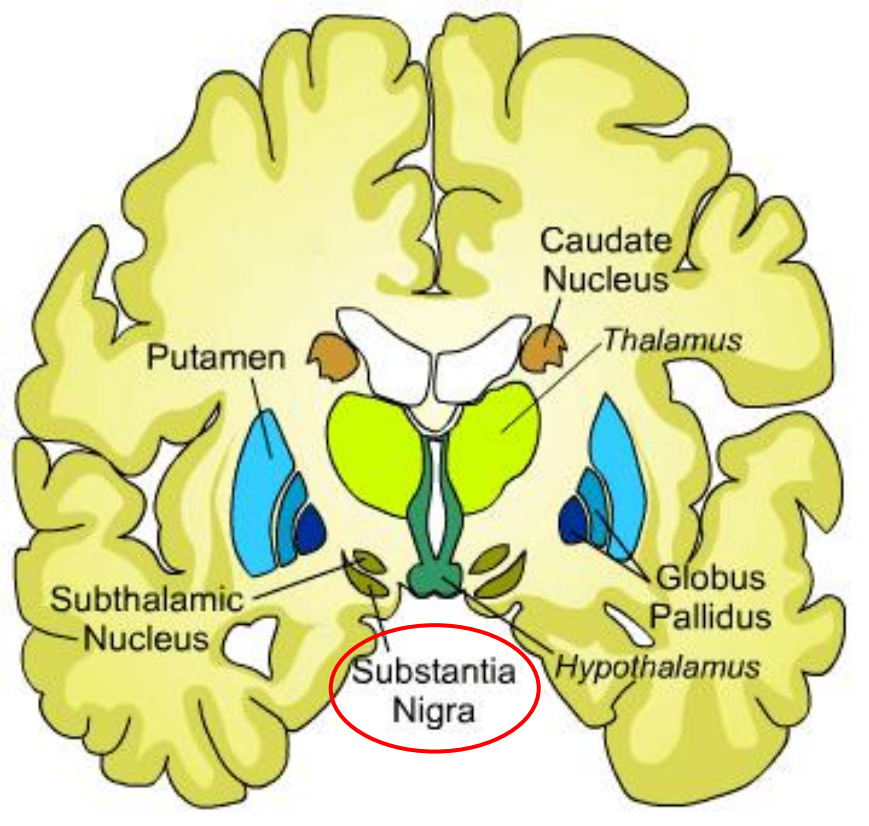
Non-motor symptoms of PD

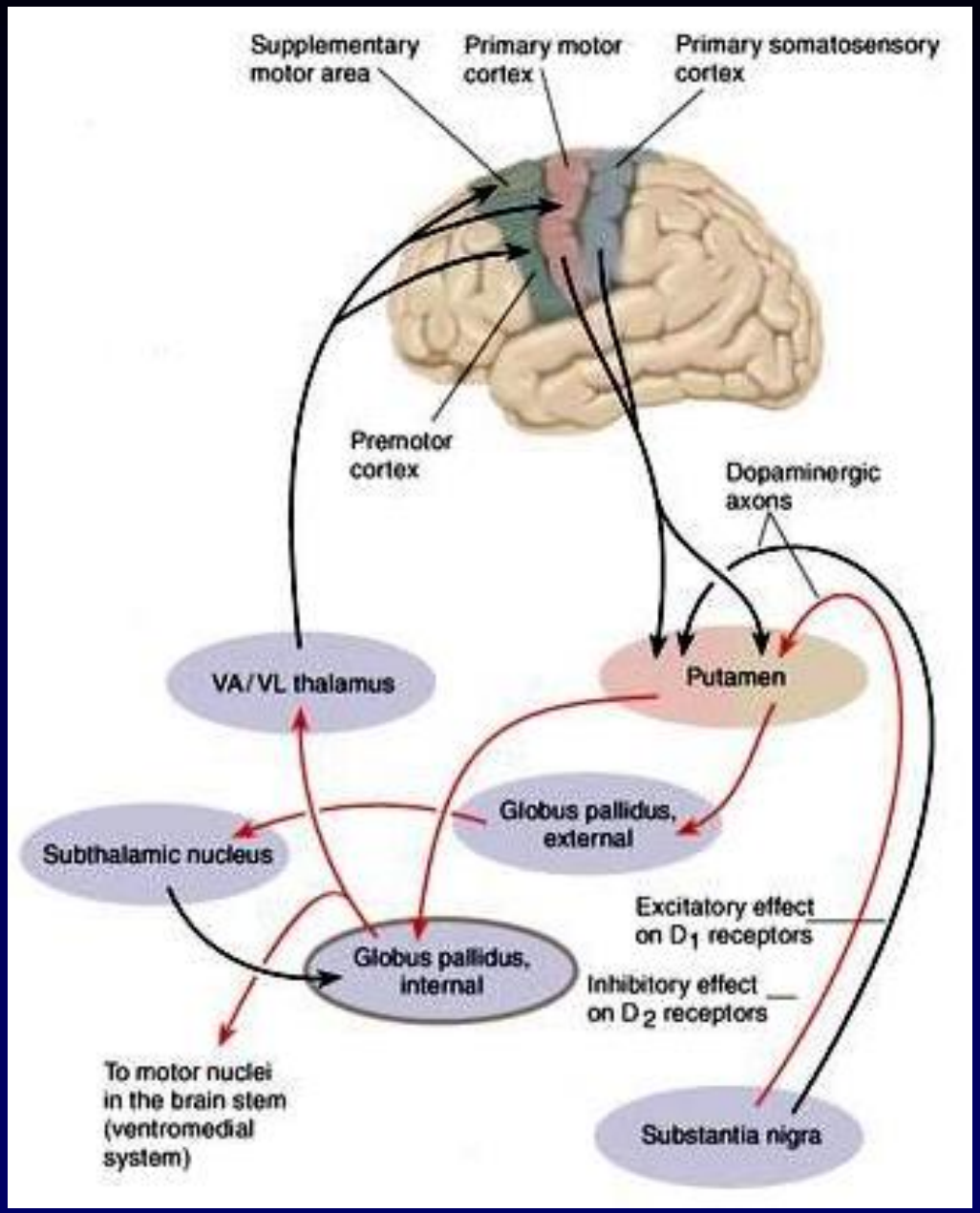
- Mood disorders (depression, anxiety, apathy)
- Cognitive disorders (memory, planning, abstract thinking, attention)
- Increased risk of dementia
- Sleep disturbance
- Low blood pressure when standing; urinary incontinence, constipation

Neuropathology of PD

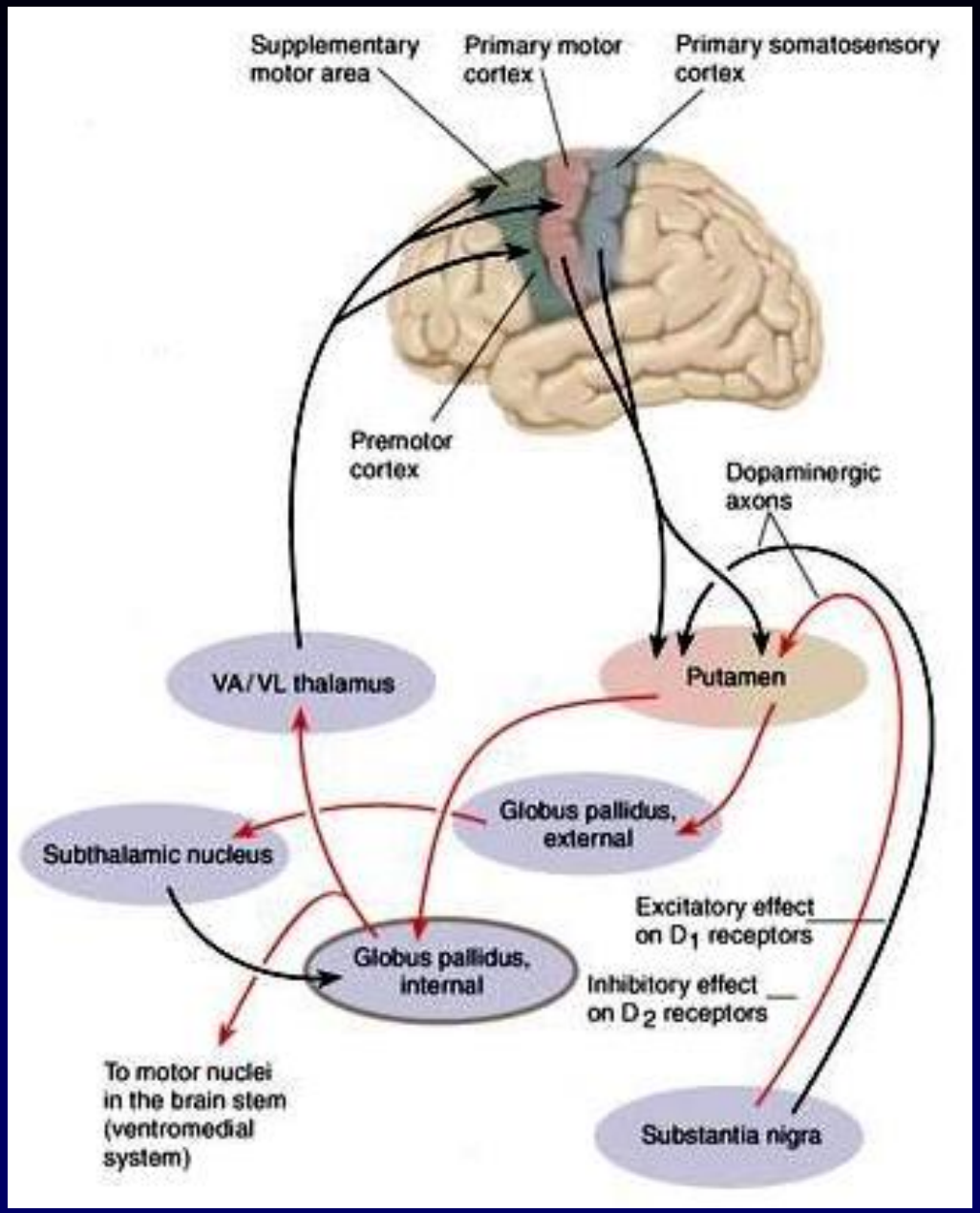
- Degeneration of the *substantia nigra* (part of basal ganglia) which produces *dopamine*





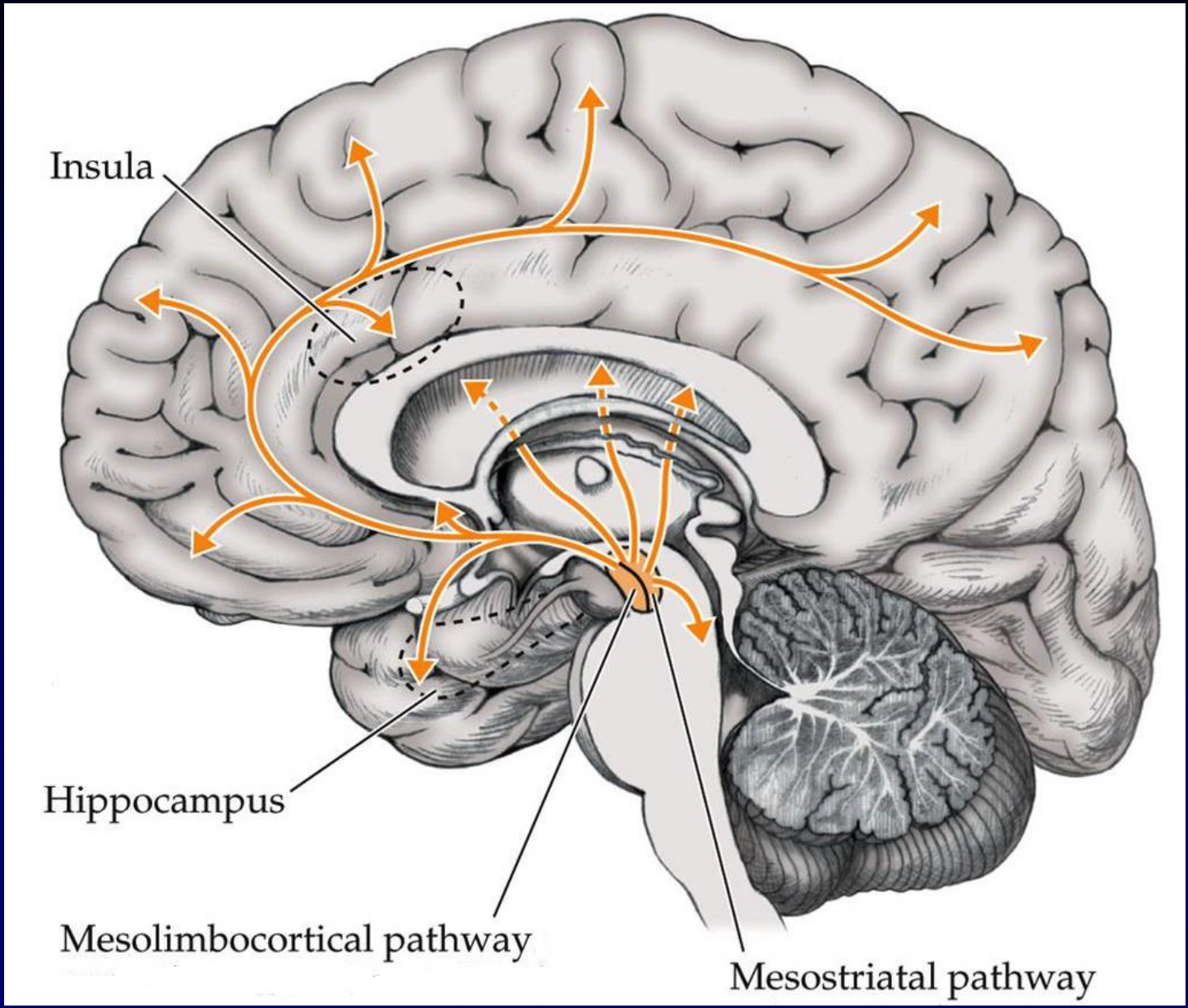


Basal Ganglia



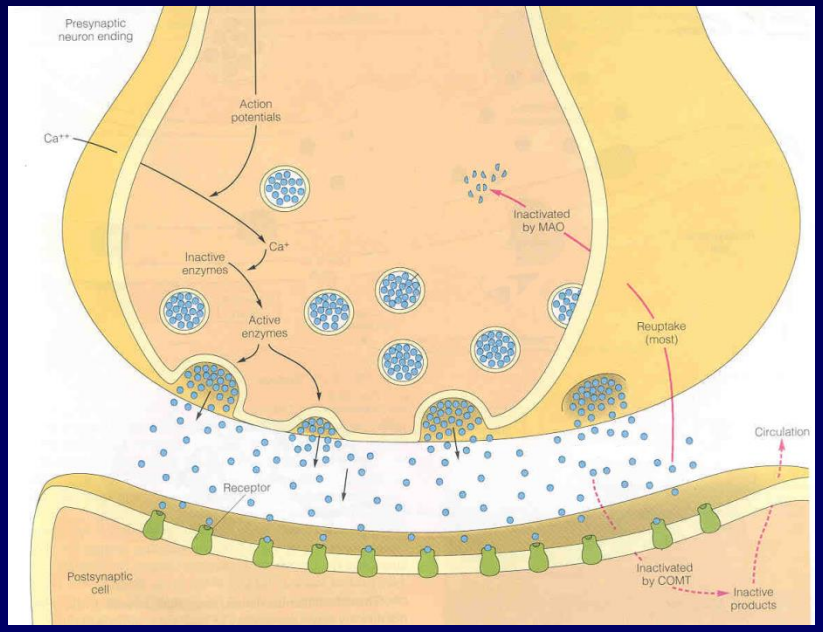
Normally, there is a balance between excitation and inhibition

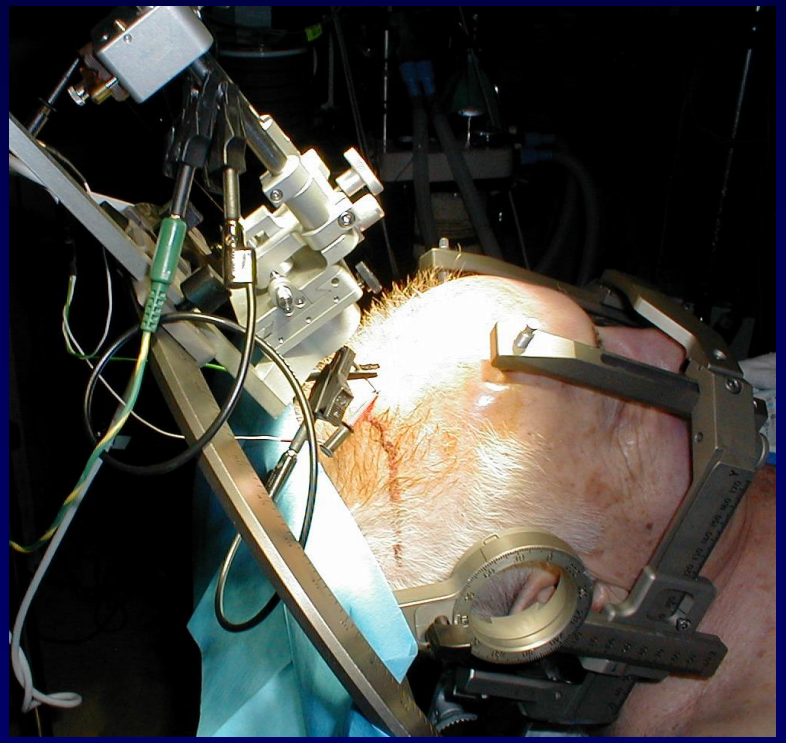
DOPAMINERGIC PATHWAYS



PD Treatments

- Medications (e.g., L-DOPA or other dopamine agonists)
- Physical, Occupational and Speech Therapy
- Treatment of non-motor symptoms
- Neurosurgery: Deep Brain Stimulation (DBS) *or* Pallidotomy





Why study auditory functions in PD patients?

- Since decreased dopamine affects so many neural networks and systems, we investigated its effects on the auditory system

- A few publications reported that PD patients exhibit deficits in auditory processing compared to age-matched subjects without PD

Previous studies of auditory function in PD patients

- Yylmaz et al. (2009): a group of **20** PD patients had worse hearing at 4000 and 8000 Hz compared to a group of **24** age-matched control subjects

Table 1 Comparison of pure tone audiometry threshold (dB) results (mean ± SD) at different frequencies for parkinsonian and control group

	250 Hz	500 Hz	1,000 Hz	2,000 Hz	4,000 Hz	8,000 Hz
20 Parkinson patient (40 ears)	22.80 ± 10.97	19.37 ± 10.51	18.25 ± 12.01	27.75 ± 18.77	44.38 ± 21.49	60.75 ± 27.23
24 control group (48 ears)	19.37 ± 8.85	16.15 ± 8.88	16.98 ± 10.35	23.33 ± 13.34	32.19 ± 17.47	50.21 ± 22.19
P	>0.05	>0.05	>0.05	>0.05	=0.04	=0.048

Mean age of PD patients = 69.9 years
Mean age of control subjects = 63.8 years

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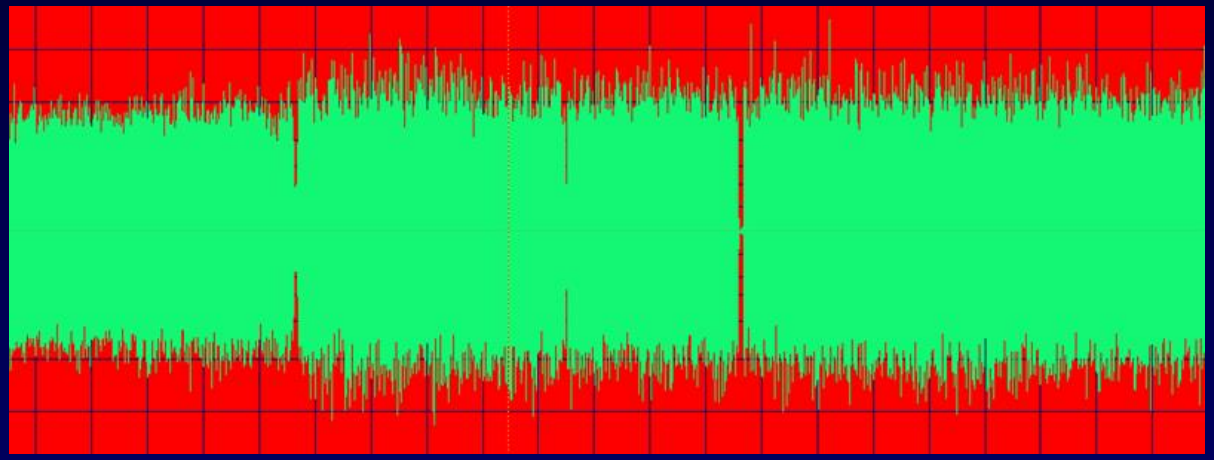
Previous studies of auditory function in PD patients

- Guehl et al. (2008): gap detection thresholds for 19 PD patients (4.4 msec) were significantly longer compared to age-matched control subjects (2.7 msec). Both groups averaged 56 years of age



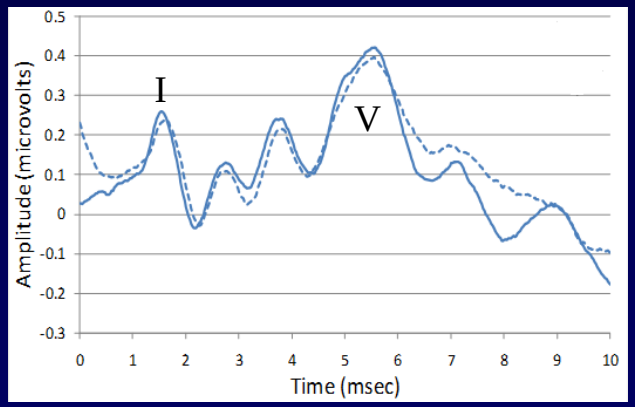
- L-DOPA did not improve the performance of PD patients, but bilateral stimulation of subthalamic nuclei improved gap detection thresholds by 10%

Previous studies of auditory function in PD patients

Lewald et al. (2004): During sound lateralization tests, the just noticeable difference (JND) in interaural time detected by PD patients was twice as long as that detected by age-matched control subjects

Previous studies of auditory function in PD patients

- Abnormal auditory brainstem responses (ABRs) in PD patients reported by
  - Tachibana et al. (1989): wave I-V inter-peak latency longer in PD patients vs. controls
  - Al-Bunyan (2000): increased latencies for waves I and V for PD patients vs. control subjects



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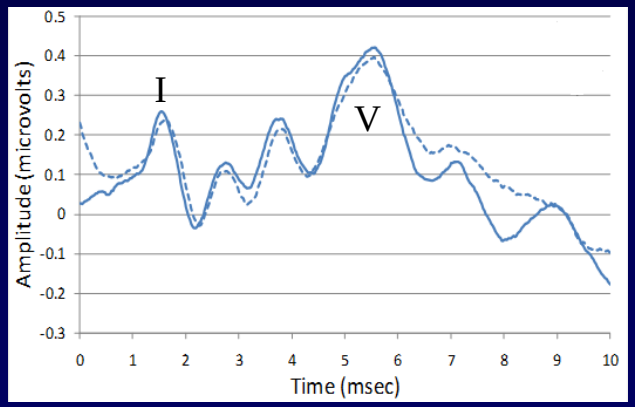
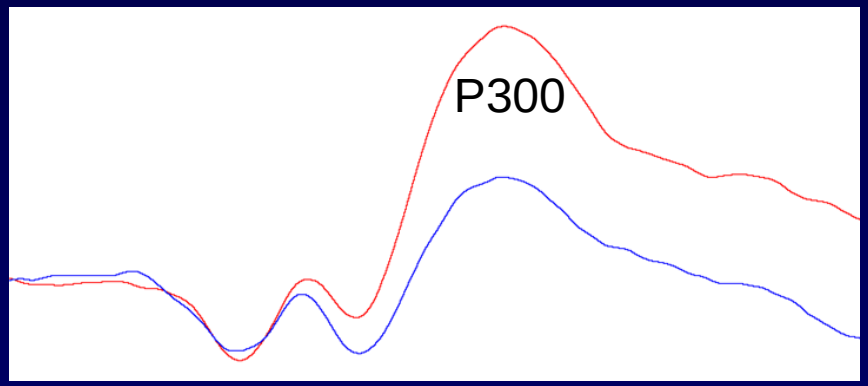


CAUTION: Hearing sensitivity of subjects was not mentioned (or evaluated?) in these studies

Previous studies of auditory function in PD patients

- Abnormal auditory P300s in PD patients reported by
  - Raudino et al. (1997) and Jiang et al. (2000): P300 amplitude was smaller in PD patients compared to healthy control subjects.
  - Hansch et al. (1982) and Katsarou et al. (2004): P300 latency was longer in PD patients compared to healthy control subjects.



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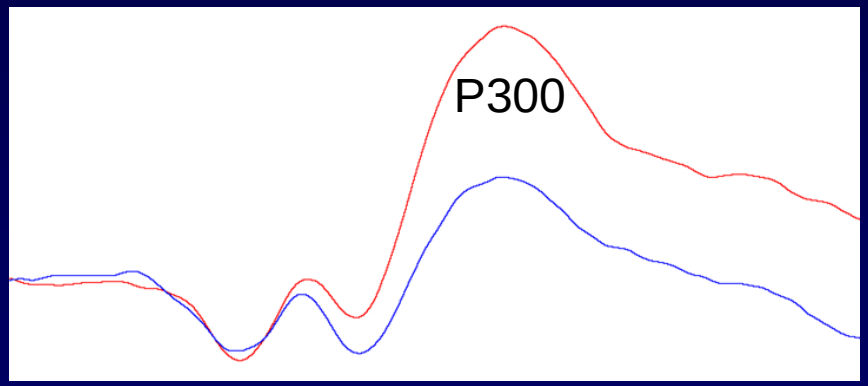

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Clinical Rehabilitation 2008; **22:** 14–22

How do I sound to me? Perceived changes in communication in Parkinson's disease

Nick Miller Institute of Health and Society, Speech language sciences, University of Newcastle, **Emma Noble** Speech language sciences, University of Newcastle, **Diana Jones** School of Health, Community and Education Studies, Northumbria University, **Liesl Allcock** Department of Geriatric Medicine, Newcastle General Hospital and **David J Burn** Institute for Ageing and Health, Newcastle University, Regional Neurosciences Centre, Newcastle General Hospital, Newcastle upon Tyne, UK

Miller et al. concluded . . .

"Across the cohort of all Parkinson's disease subjects completing the questionnaire, there was a statistically significant perception of deterioration in communication after the onset of Parkinson's disease."

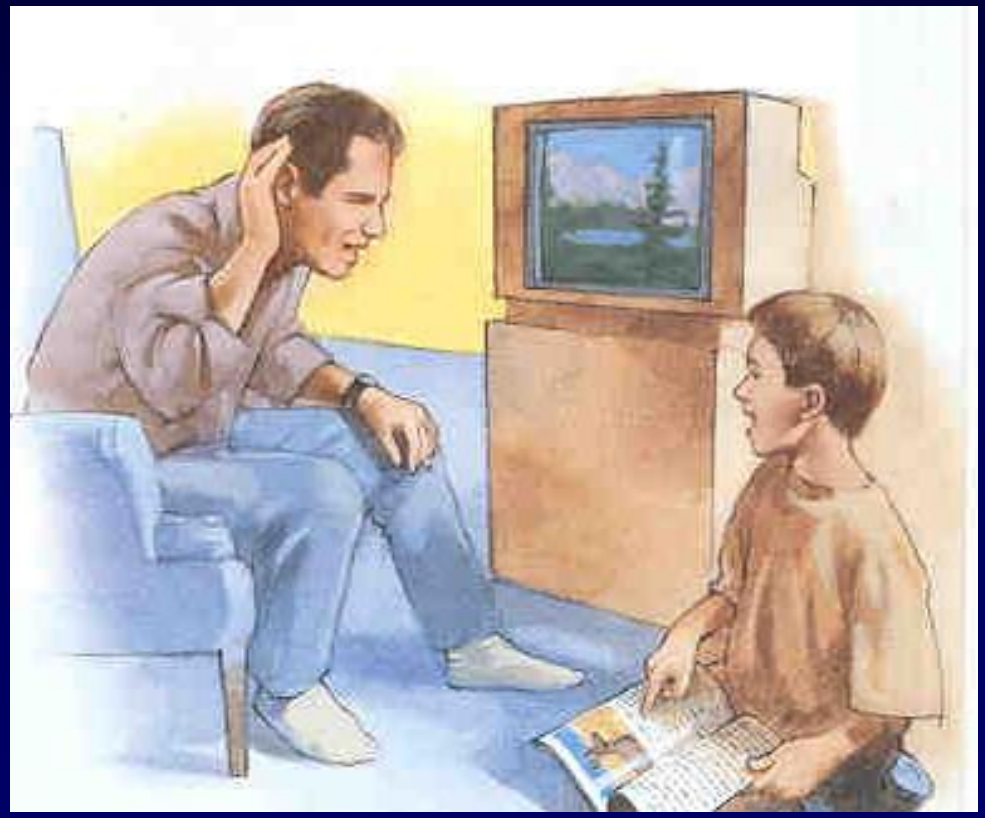
"The main finding of this study is that, almost without exception, Parkinson's disease exercises a negative influence on communication, irrespective of age and gender."

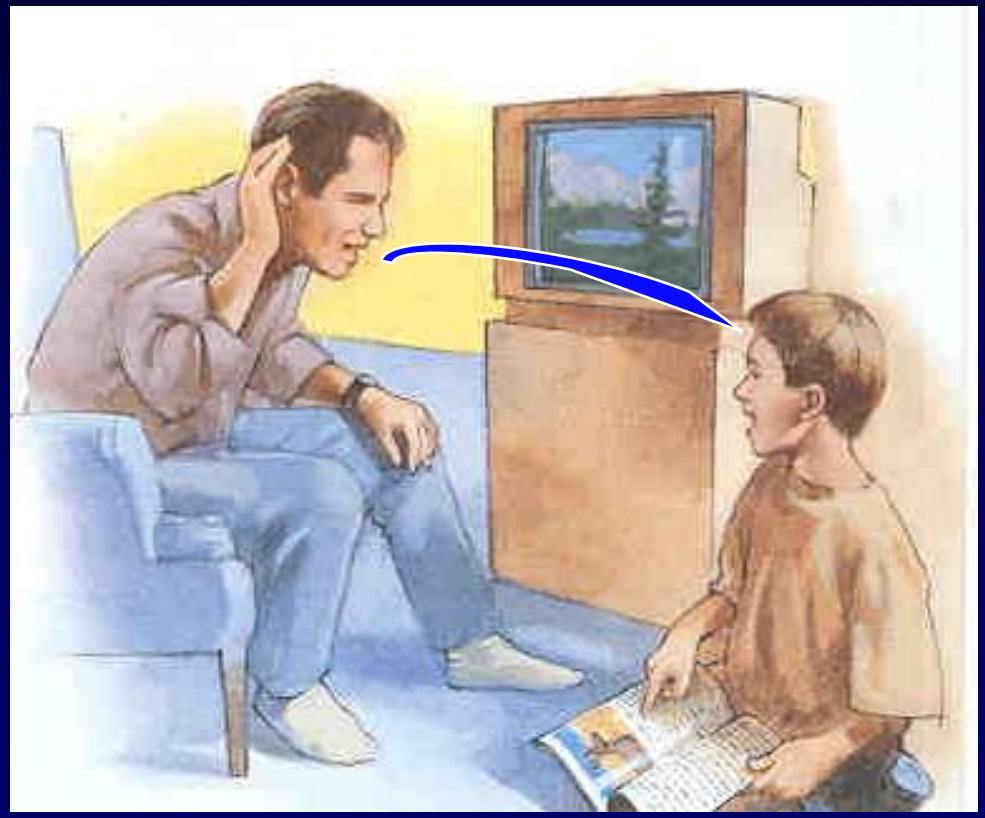
Miller et al. concluded . . .

"Across the cohort of all Parkinson's disease subjects completing the questionnaire, there was a statistically significant perception of deterioration in communication after the onset of Parkinson's disease."

"The main finding of this study is that, almost without exception, Parkinson's disease exercises a negative influence on communication, irrespective of age and gender."

Hearing ability/sensitivity is not mentioned <u>at all</u> in the article, even though the mean age of PD patients was 71.6 ± 8.4 years *!*





2-Year Project at NCRAR

- funded by VA RR&D Service

Study Team

- Robert Folmer, Ph.D. – P.I.
- Jay Vachhani, Au.D. – Research Audiologist
- John Nutt, M.D. – Co-Investigator
- Kathy Chung, M.D. – Co-Investigator
- Dan Storzbach, Ph.D. – Neuropsychologist
- Garnett McMillan, Ph.D. – Biostatistician

Study Subjects

Parkinson Patients (n=35; 12 females)

- Absence of current major disease other than PD
- Mean age = 66.6 years
- Mean duration of PD = 7 years
- Mean Hoehn & Yahr stage = 1.7 (range = 1-3)
- Mean Schwab & England score = 86.2% (range = 70-100%)

Control Subjects (n=35; 4 females)

- Absence of neurological disorder, diabetes
- Mean age = 66.0 years

Study Protocols

1. Questionnaires
2. Neuropsychological Assessments
3. Audiometric Evaluations
4. Behavioral Central Auditory Processing (CAP) Tests
5. Electrophysiological Assessments
   (Auditory event-related potentials)

Study Protocols

Questionnaires

- World Health Organization Disability Assessment Schedule (WHODAS II)
- Medical History and Hearing History questionnaires
- Hearing Handicap Inventory for Adults (HHIA)

World Health Organization Disability Assessment Schedule (WHODAS II)

7 Areas: Understanding & Communicating (Cognition)
Getting Around (Mobility)
Self-Care
Getting Along With People
Life Activities (Household)
Life Activities (Work)
Participation in Society

World Health Organization Disability Assessment Schedule (WHODAS II)

Total Score

PD Patients: 48.6 ± 11.8

Control Subjects: 38.7 ± 10.3

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$p = 0.0009$

World Health Organization Disability Assessment Schedule (WHODAS II)

Total Score

PD Patients: 48.6 ± 11.8

Control Subjects: 38.7 ± 10.3

$p = 0.0009$

Biggest contributors to this difference:

Participation in Society (40%)

Mobility (18%)

Cognition/Communication (14%)

Household Activities (14%)

Hearing History Questionnaire

Do you have difficulty hearing the words people are speaking?

	OFTEN	SOMETIMES	NO
PD PATIENTS	11 (31%)	15 (43%)	9 (26%)
CONTROL SUBJECTS	2 (6%)	24 (69%)	9 (26%)

Hearing Handicap Inventory for Adults (HHIA)

	4 pts	2 pts	0 pts
S-1. Does a hearing problem cause you to use the phone less often than you would like?	○ Yes	○ Sometimes	○ No
E-2. Does a hearing problem cause you to feel embarrassed when meeting new people?	○ Yes	○ Sometimes	○ No
S-3. Does a hearing problem cause you to avoid groups of people?	○ Yes	○ Sometimes	○ No
E-4. Does a hearing problem make you irritable?	○ Yes	○ Sometimes	○ No
E-5. Does a hearing problem cause you to feel frustrated when talking to members of your family?	○ Yes	○ Sometimes	○ No
S-6. Does a hearing problem cause you difficulty when attending a party?	○ Yes	○ Sometimes	○ No
E-7. Does a hearing problem cause you to feel frustrated when talking to coworkers, clients or customers?	○ Yes	○ Sometimes	○ No
S-8 Does a hearing problem cause you difficulty in the movies or theater?	○ Yes	○ Sometimes	○ No
E-9. Do you feel handicapped by a hearing problem?	○ Yes	○ Sometimes	○ No
S-10. Does a hearing problem cause you difficulty when visiting friends, relatives, or neighbors?	○ Yes	○ Sometimes	○ No
	Total: _____	_____	_____

Hearing Handicap Inventory for Adults (HHIA)

PD Patients: 18.6 ± 18.5

Control Subjects: 15.0 ± 17.1

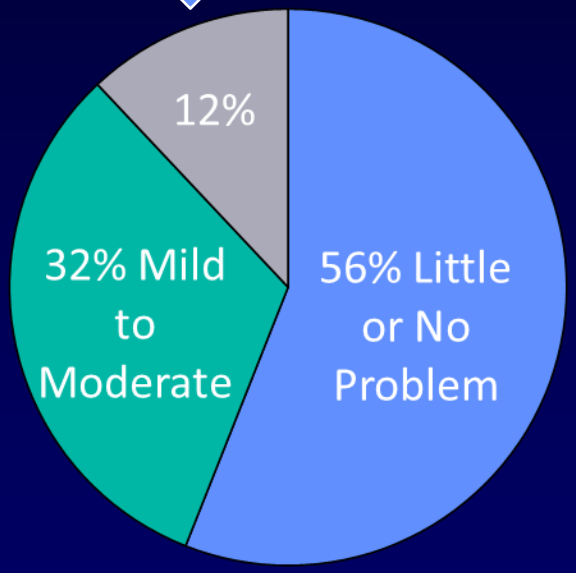
- no significant difference

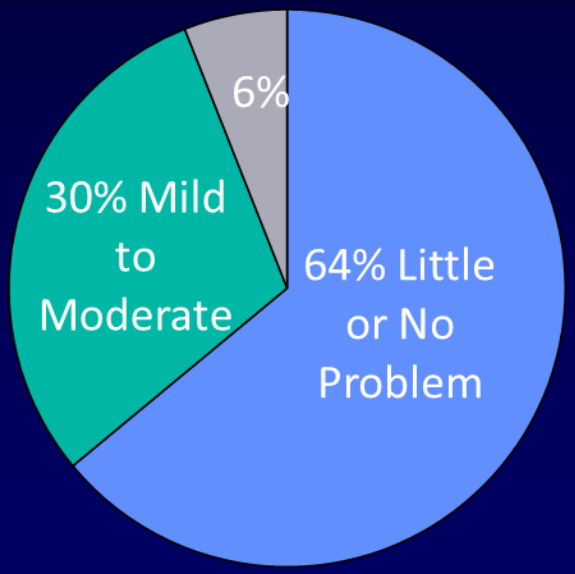
Hearing Handicap Inventory for Adults (HHIA)

PD Patients

Control Subjects

Severe Problem





Study Protocols

Neuropsychological Assessments

- Rey Auditory Verbal Learning Test (Rey, 1941): assesses short-term memory and learning

- Wide Range Achievement Test (WRAT-Reading): assesses word reading ability

- Beck Depression Inventory II (Beck et al, 1996): patient-administered questionnaire

Results

Neuropsychological Assessments

- Rey Auditory Verbal Learning Test:
  PD Patients: 42 ± 9 Control Subjects: 46 ± 11

- Wide Range Achievement Test:
  PD Patients: 63 ± 6 Control Subjects: 65 ± 7

- Beck Depression Inventory:
  PD Patients: 7 ± 5 Control Subjects: 5 ± 6

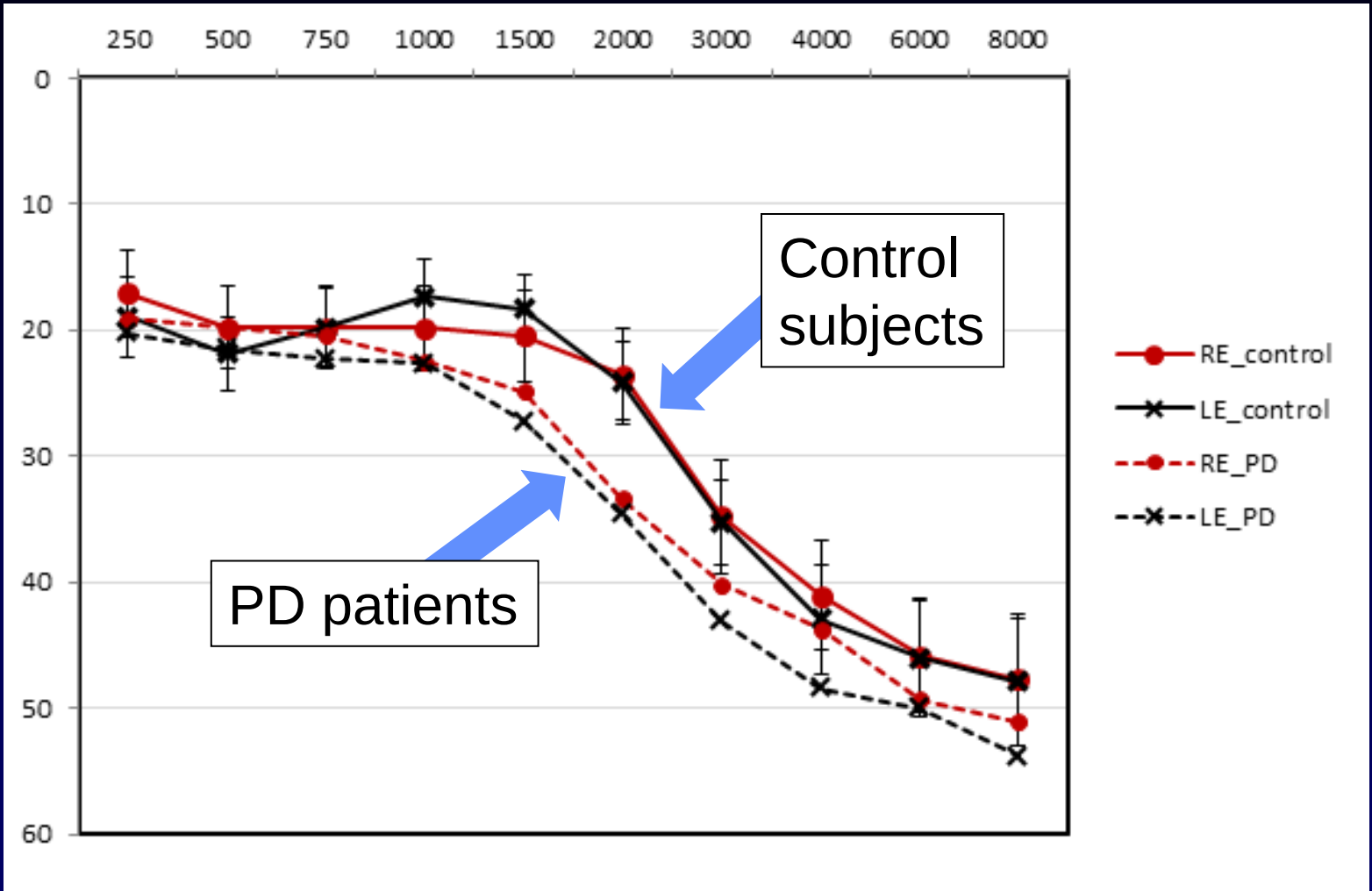
Education Levels of Study Participants

Control Subjects: 20 of 35 (57%) earned bachelor's or higher degrees

Parkinson Patients: 27 of 35 (77%) earned bachelor's or higher degrees

(in Multnomah and Washington counties, Oregon 49% of the adult population have bachelor's or higher degrees)

Pure Tone Audiometric Results



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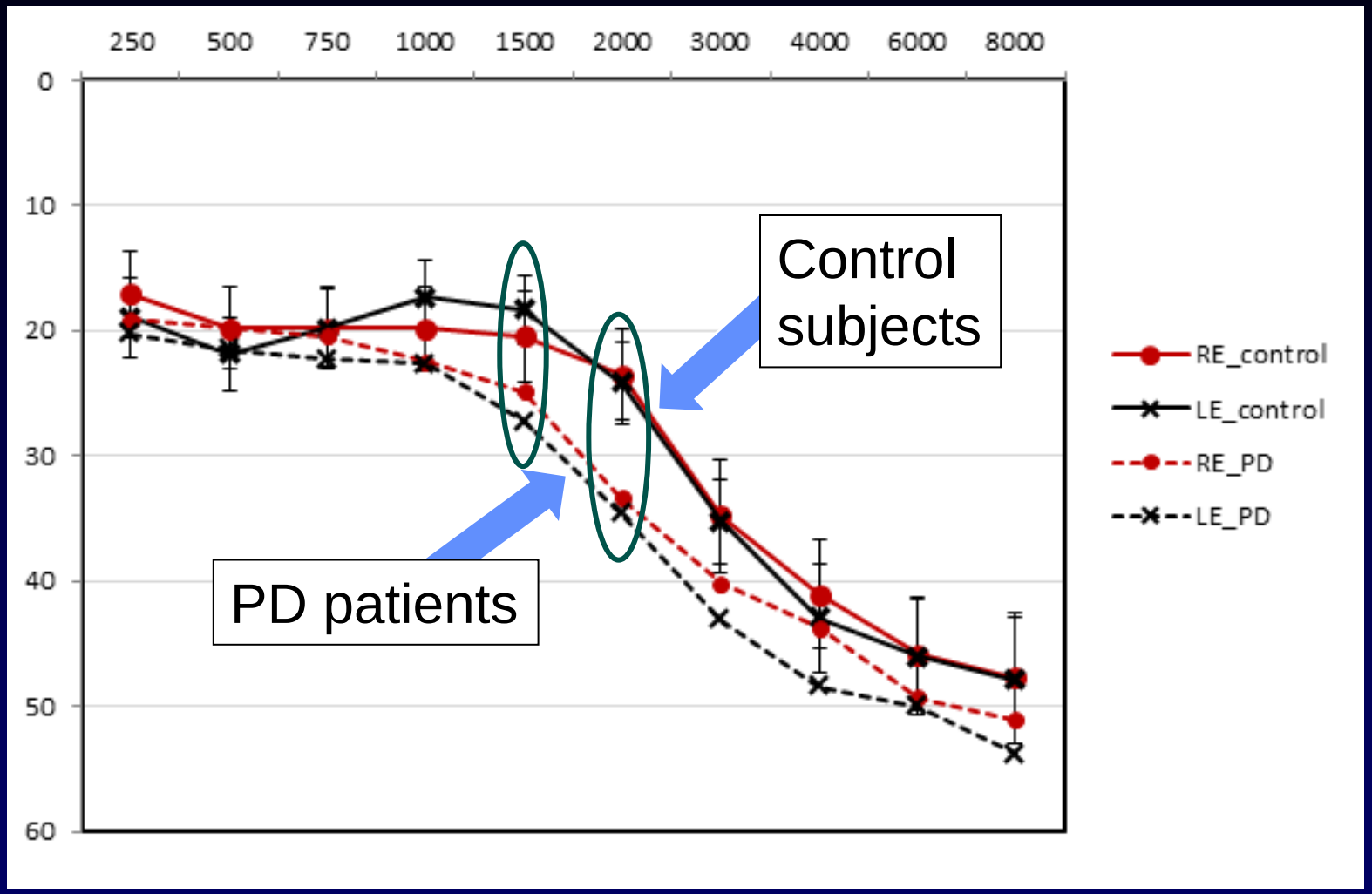

Significantly worse hearing for PD patients at 1500 and 2000 Hz in both ears

Why are these results different from those reported by Yylmaz et al. in 2009?

(their PD patients had worse hearing at 4000 and 8000 Hz compared to age-matched control subjects)

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(their PD patients had worse hearing at 4000 and 8000 Hz compared to age-matched control subjects)

- **Small sample sizes:**
  20 PD patients / 24 control subjects for Yylmaz
  35 PD patients / 35 control subjects in our study

Audiometric Results

Based on our audiometric results,
27 of 35 PD Patients are good candidates for amplification (77%)

- Of these 27 hearing aid candidates,
  only 7 used hearing aids (26%)

19 of 35 Control Subjects are good candidates for amplification (54%)

- Of these 19 hearing aid candidates,
  11 used hearing aids (58%)

Central Auditory Processing (CAP) Tests

- Staggered-Spondaic-Word (SSW) test (Katz, 1998)
- Gaps in Noise test (Musiek et al., 2005)
- Masking-Level Difference (MLD) test (Hirsh, 1948)
- Dichotic Digits Test (Musiek, 1983)
- Frequency Pattern Sequence Test (Musiek & Pinheiro, 1987)
- Words in Noise (WIN) Test (Wilson & Burks, 2005)
- Spatial Release from Masking (SRM) Test (Bolia, 2000; Gallun, 2013)

STAGGERED SPONDAIC WORD TEST (SSW)

Fruit

Juice

Cup

Cake

Four Test Conditions:

Right non-competing (RNC)

Right competing (RC)

Left competing (LC)

Left non-competing (LNC)

STAGGERED SPONDAIC WORD TEST (SSW)

Fruit

Juice

Cup

Cake

Four Test Conditions:

Left non-competing (LNC)

Left competing (LC)

Right competing (RC)

Right non-competing (RNC)

STAGGERED SPONDAIC WORD TEST (SSW)

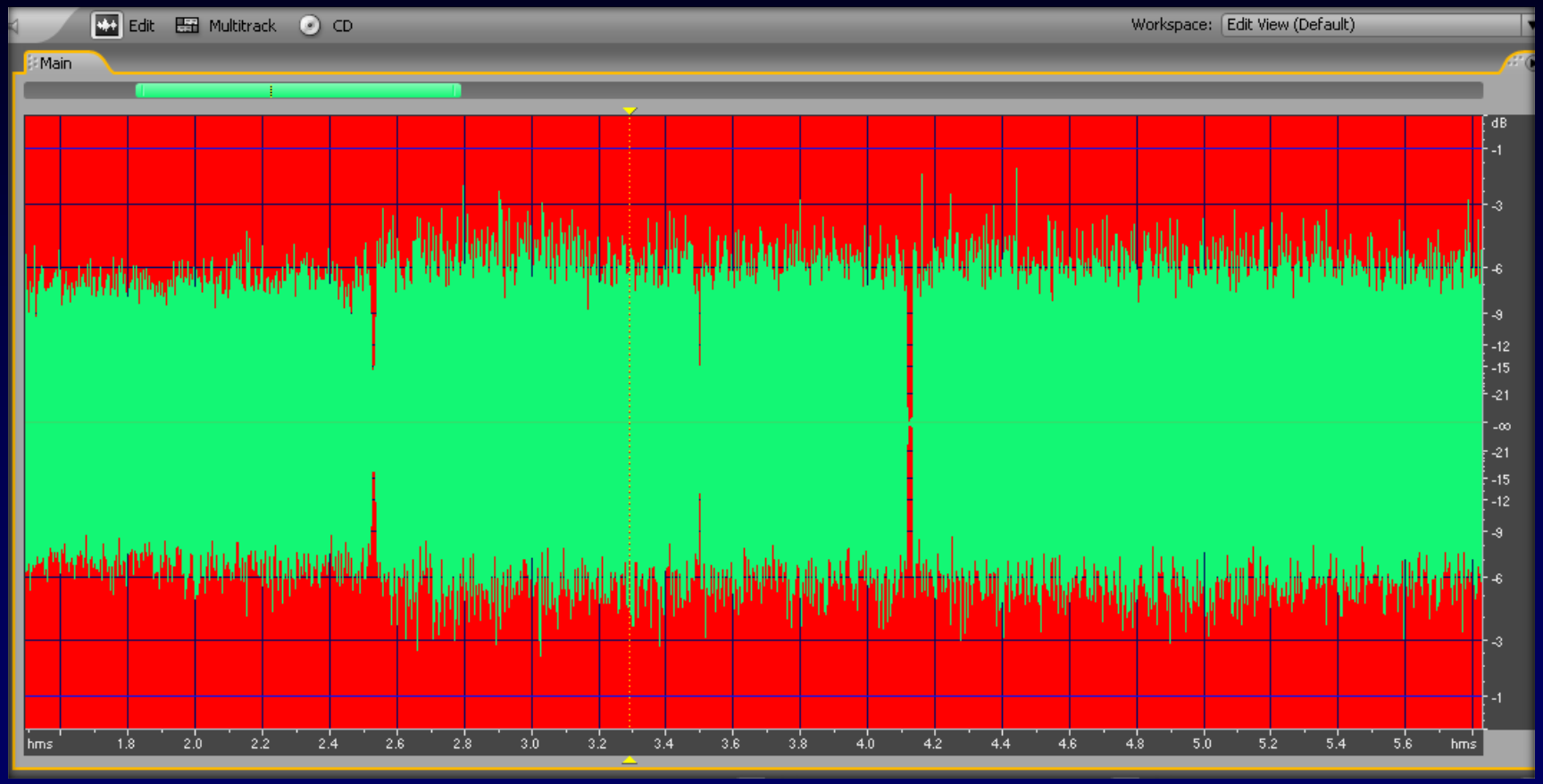
TOTAL ERRORS

PD Patients: 14.4 ± 12.2

Control Subjects: 13.8 ± 16.5

Normal outcome for this test
is 10 or fewer errors for people with normal hearing
or mild hearing loss

GAPS IN NOISE (GIN) DETECTION TEST



GAPS IN NOISE (GIN) DETECTION TEST

	LEFT EAR GAP THRESHOLD	RIGHT EAR GAP THRESHOLD
PD PATIENTS	9.7 ± 3.4 msec	8.9 ± 3.5 msec
CONTROL SUBJECTS	8.9 ± 4.5 msec	8.7 ± 4.8 msec

Normal Gap Detection Threshold for this test is ≤ 8 msec for people with normal hearing or mild hearing loss

DICHOTIC DIGITS TEST

4, 7

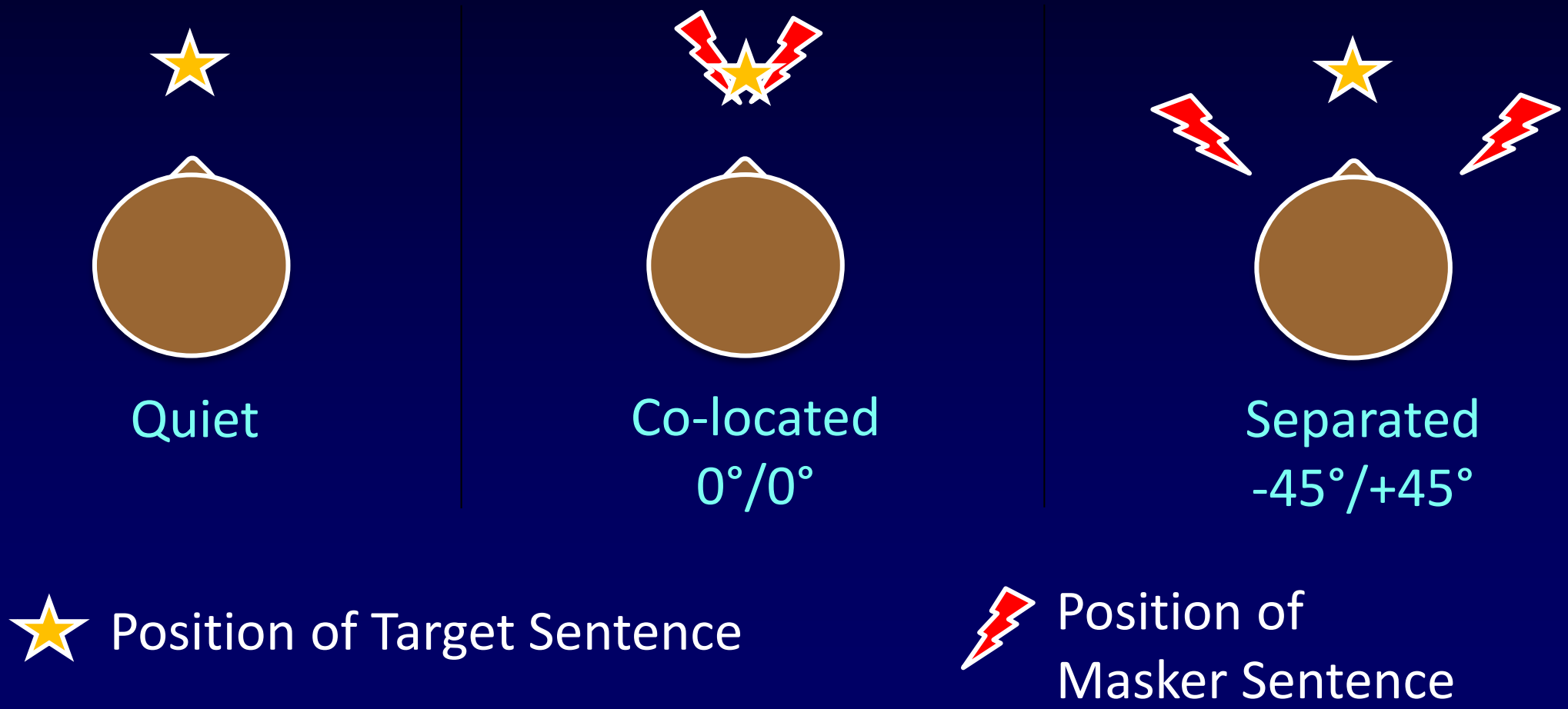
5, 2

DICHOTIC DIGITS TEST

	LEFT EAR % CORRECT	RIGHT EAR % CORRECT
PD PATIENTS	86 ± 12%	93 ± 13%
CONTROL SUBJECTS	84 ± 13%	88 ± 14%

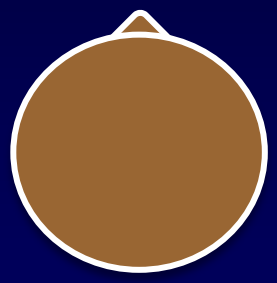
Normal outcome for this test
is ≥ 90% correct for people with normal hearing
or mild hearing loss

Spatial Release from Masking (SRM) Test



Spatial Release from Masking (SRM) Test

Ready Charlie go to red five now.

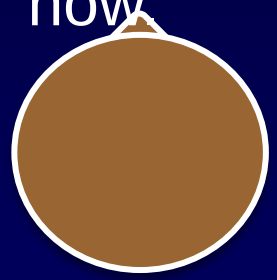


Quiet

Ready Tiger go to green eight now.

Ready Ringo go to blue two now.

Ready Charlie go to red five now.

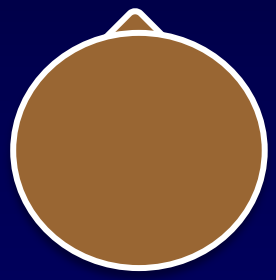


Co-located
0°/0°

Ready Charlie go to red five now.

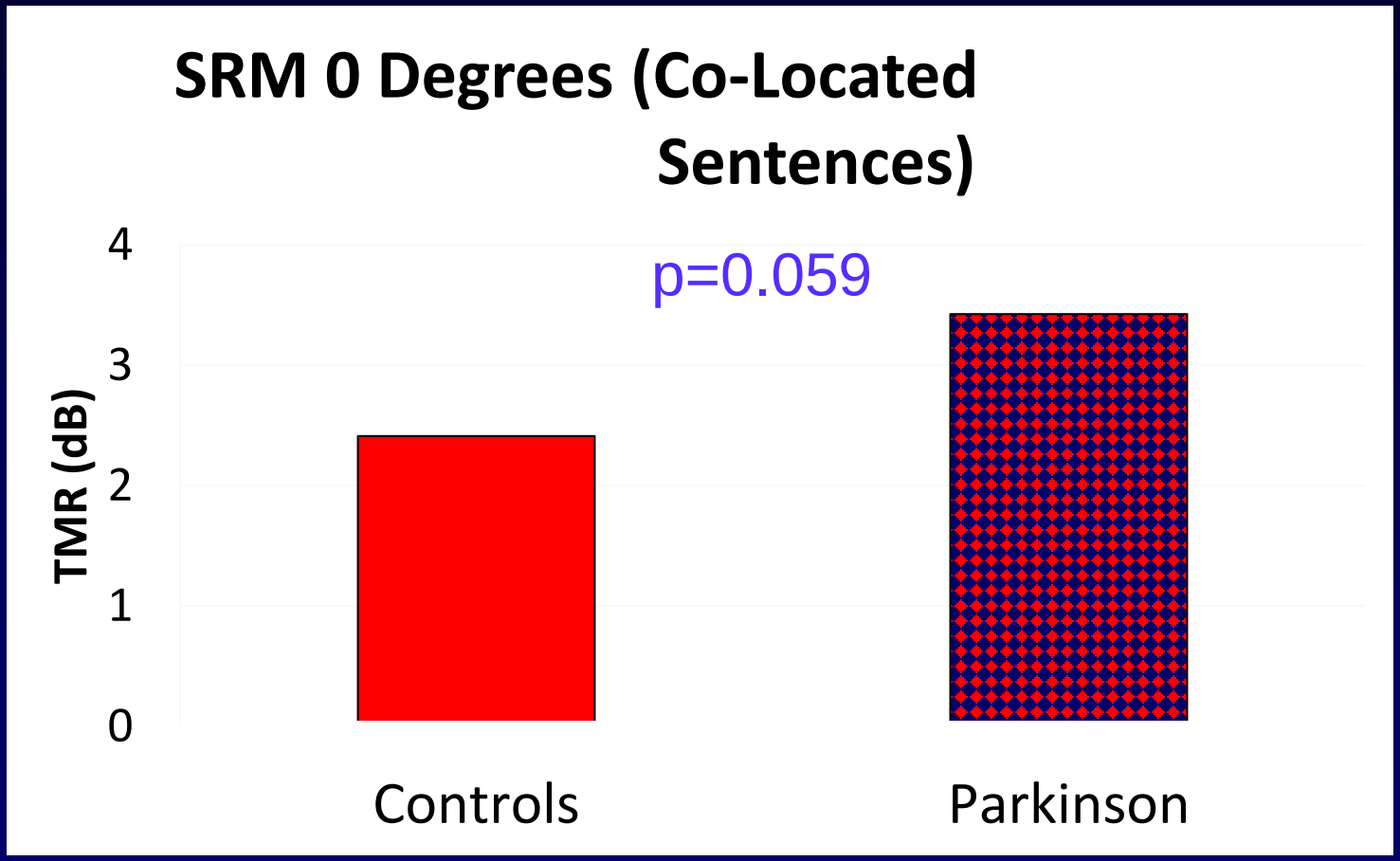
Ready Tiger go to green eight now.

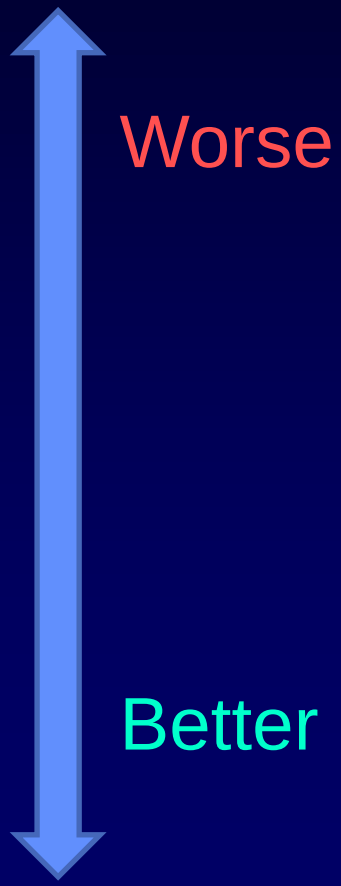
Ready Ringo go to blue two now.



Separated
-45°/+45°

Spatial Release from Masking (SRM) Test





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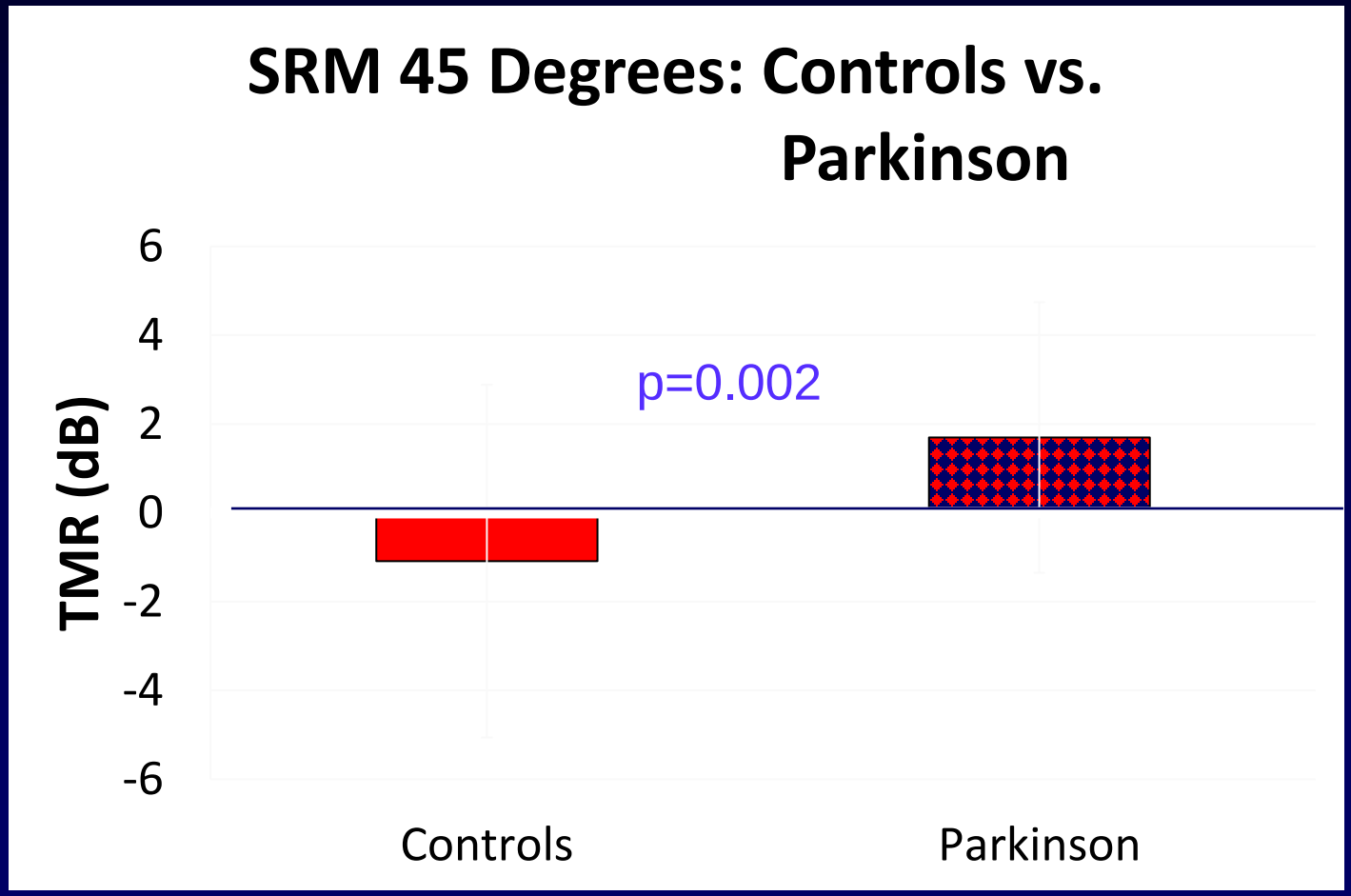
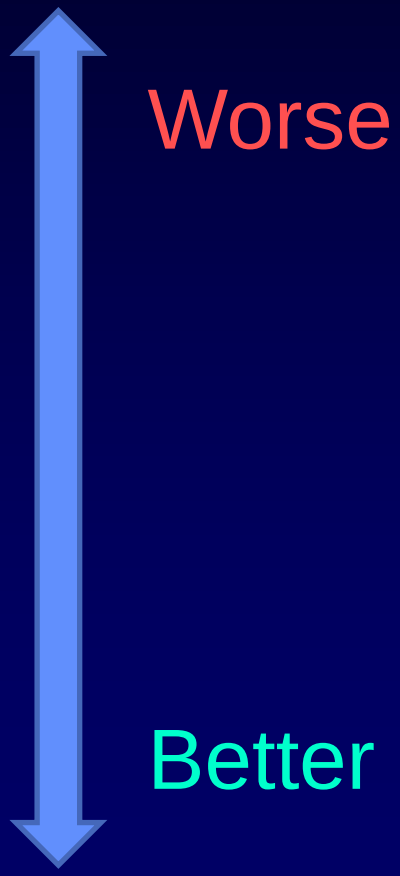




Central Auditory Processing (CAP) Tests

Results: The only significant group differences between PD Patients and Control Subjects were on the Spatial Release from Masking Tests

Why?

Central Auditory Processing (CAP) Tests

Results: The only significant group differences between PD Patients and Control Subjects were on the Spatial Release from Masking Tests

Why?

- The progression/severity of our patients' PD might not yet contribute to many central auditory processing deficits beyond the effects of aging and hearing loss

- Only the SRM test has sufficient sensitivity to differentiate these populations

Electrophysiological Protocols

- Auditory Brainstem Response (ABR)
- Long-Latency Auditory Event-Related Potentials (AERPs)
  - Auditory P300 (“Oddball” paradigm)
  - Dichotic Digits

Electrophysiological Protocols

- Auditory Brainstem Responses (ABRs) were recorded in response to monaural and binaural click stimuli

Results: No significant differences in ABR component latencies or amplitudes between groups

Why did previous studies report differences in ABRs?

Electrophysiological Protocols

- Auditory Brainstem Responses (ABRs) were recorded in response to monaural and binaural click stimuli

Results: No significant differences in ABR component latencies or amplitudes between groups

Why did previous studies report differences in ABRs?

Small study populations; ABR recording parameters; hearing sensitivity not considered or tested

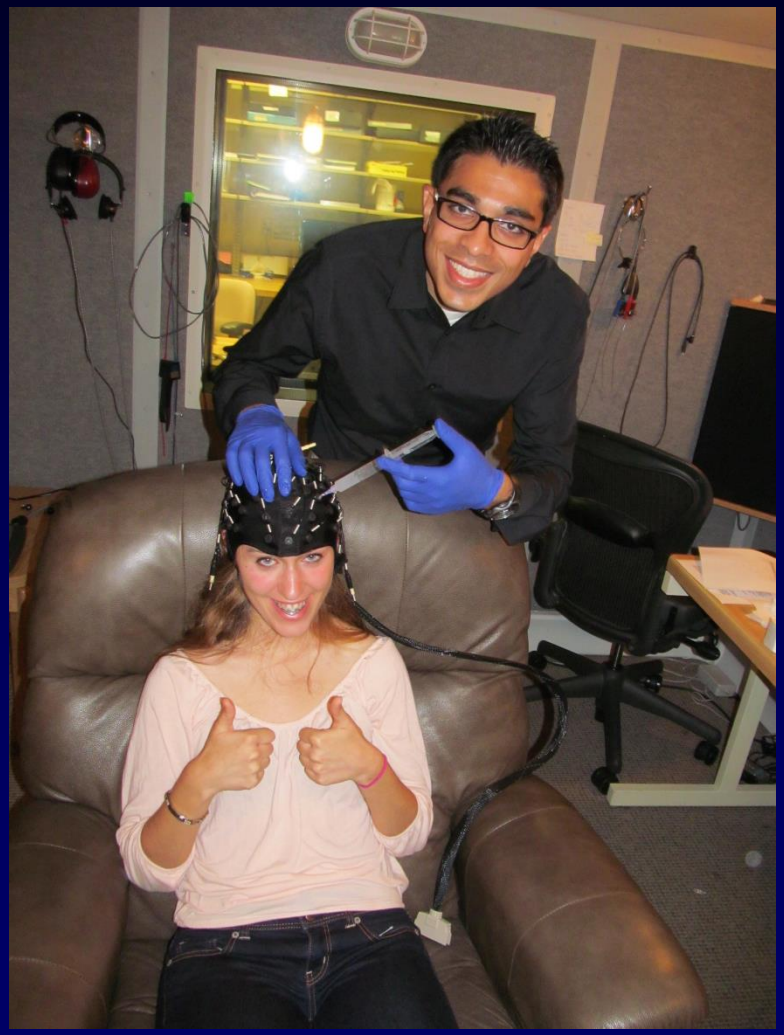
Electrophysiological Protocols

- Long-Latency Auditory Event-Related Potentials

Auditory P300 ("Oddball" paradigm)

Stimuli:	100 ms duration tones 85 dB SPL, ISI = 1.5 msec 200 (80%) 500 Hz non-target tones 50 (20%) 1000 Hz target tones
Presentation:	Monaural through insert earphones Two runs (250 sweeps) in R / L ears
Recording:	15 scalp electrodes Gain = 100,000 LF cutoff = 0.05 Hz HF cutoff = 100 Hz Rejection rate = 6 dB / octave
Subjects' task:	Count high-pitched tones silently to themselves

Long-Latency AERPs Electrophysiology Setup

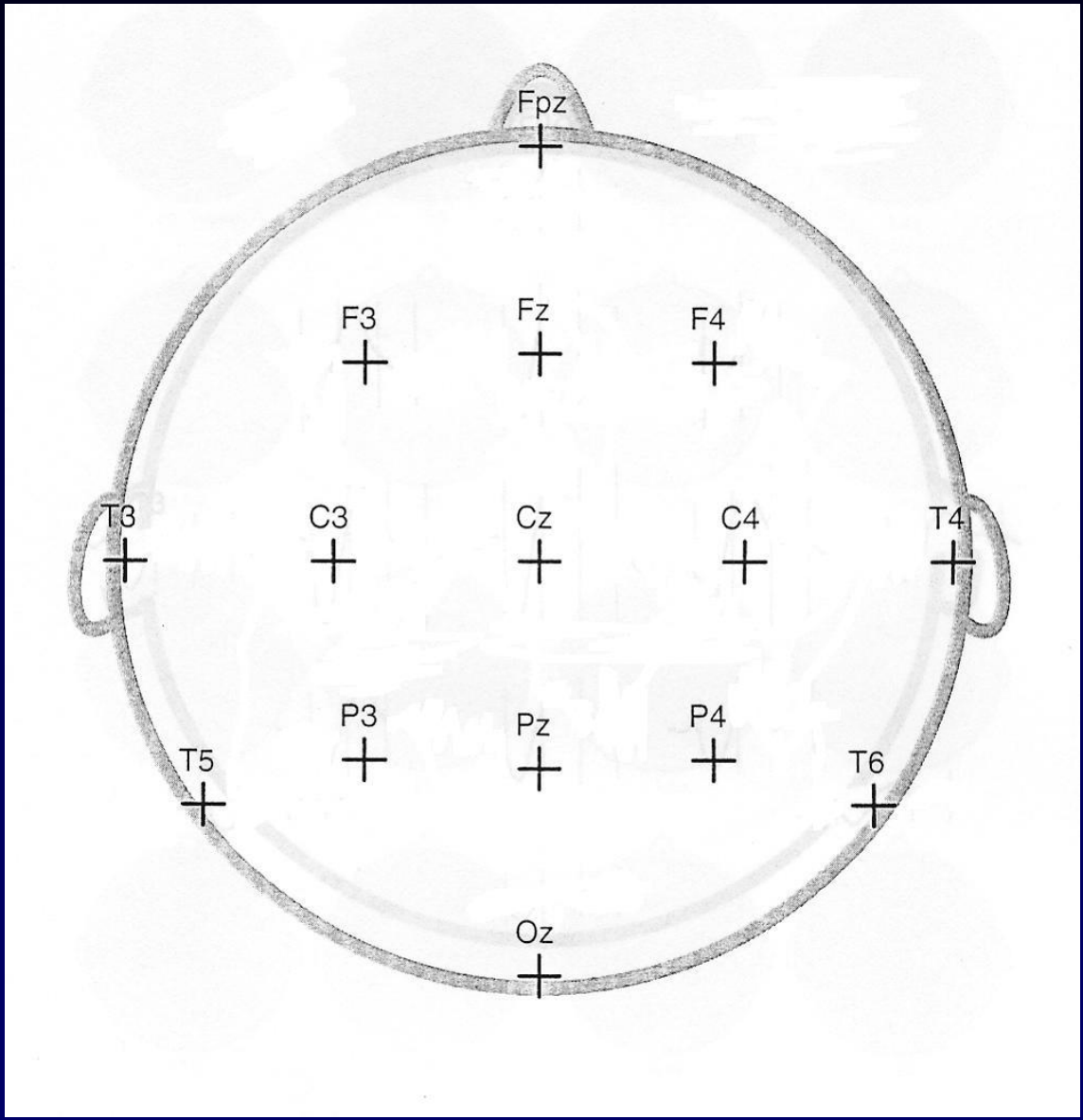


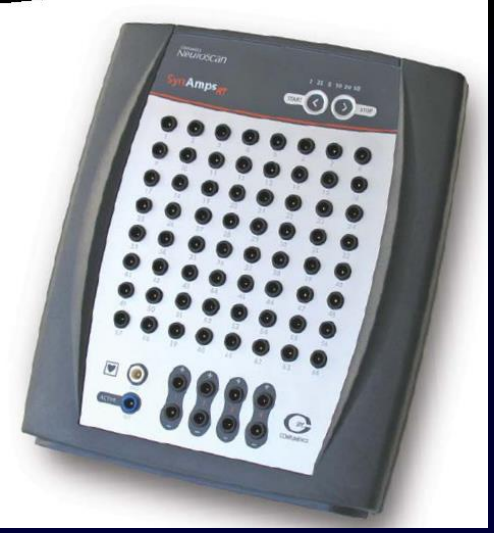
Apply Neuroscan Quik Cap and inject conductive gel with a blunt syringe

Recording sites:

- 15 scalp electrodes referenced to the subject's nose
- + 2 EOG channels

Scalp Electrode Positions





www.neuroscan.com

Neuroscan Setup

Scalp electrodes connected to non-inverting inputs of differential preamplifiers

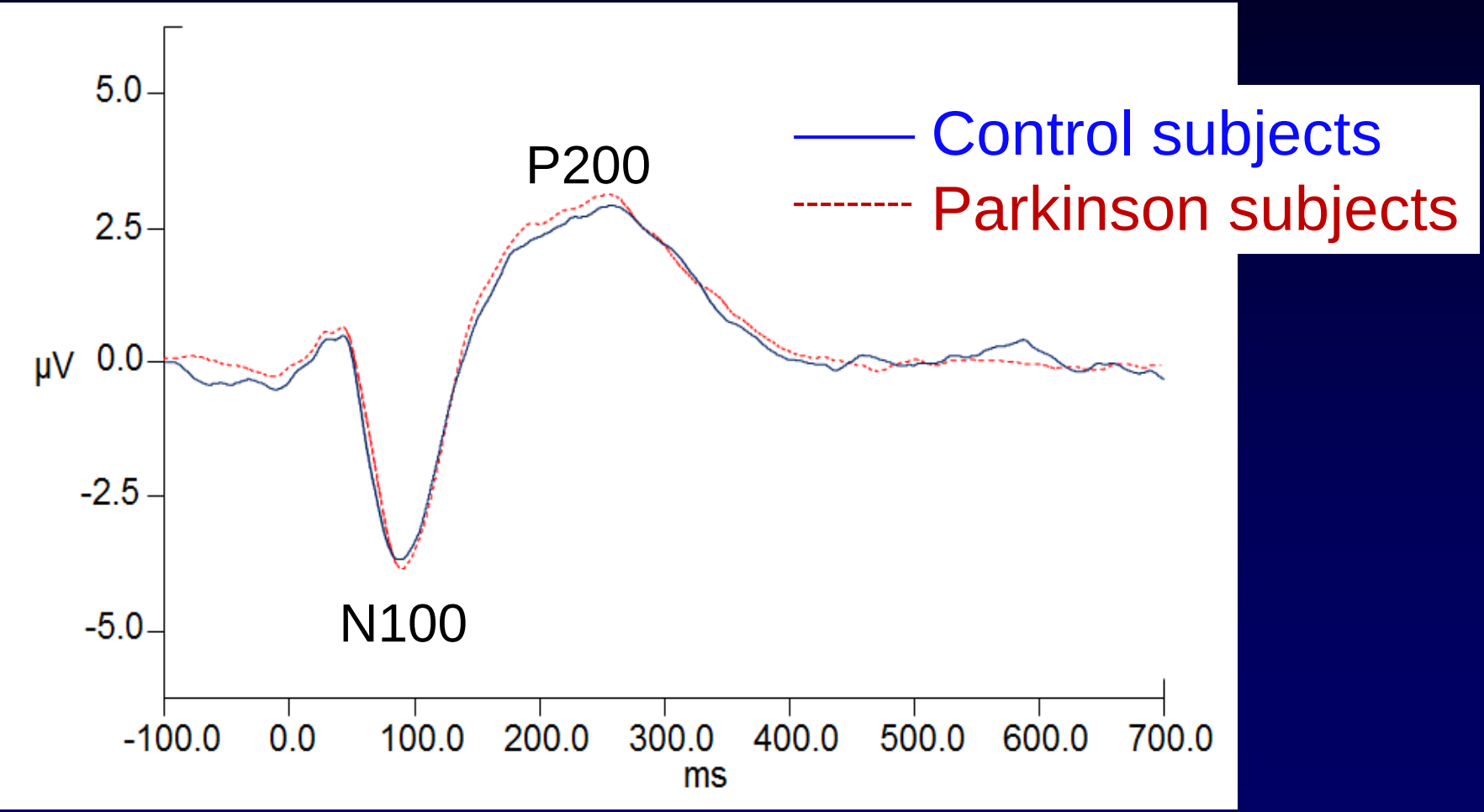
www.neuroscan.com

Electrodes also attached above and below the left eye and lateral to each outer canthus to track eye movements

Eye movements greater than 60 µV were excluded from AERP averages

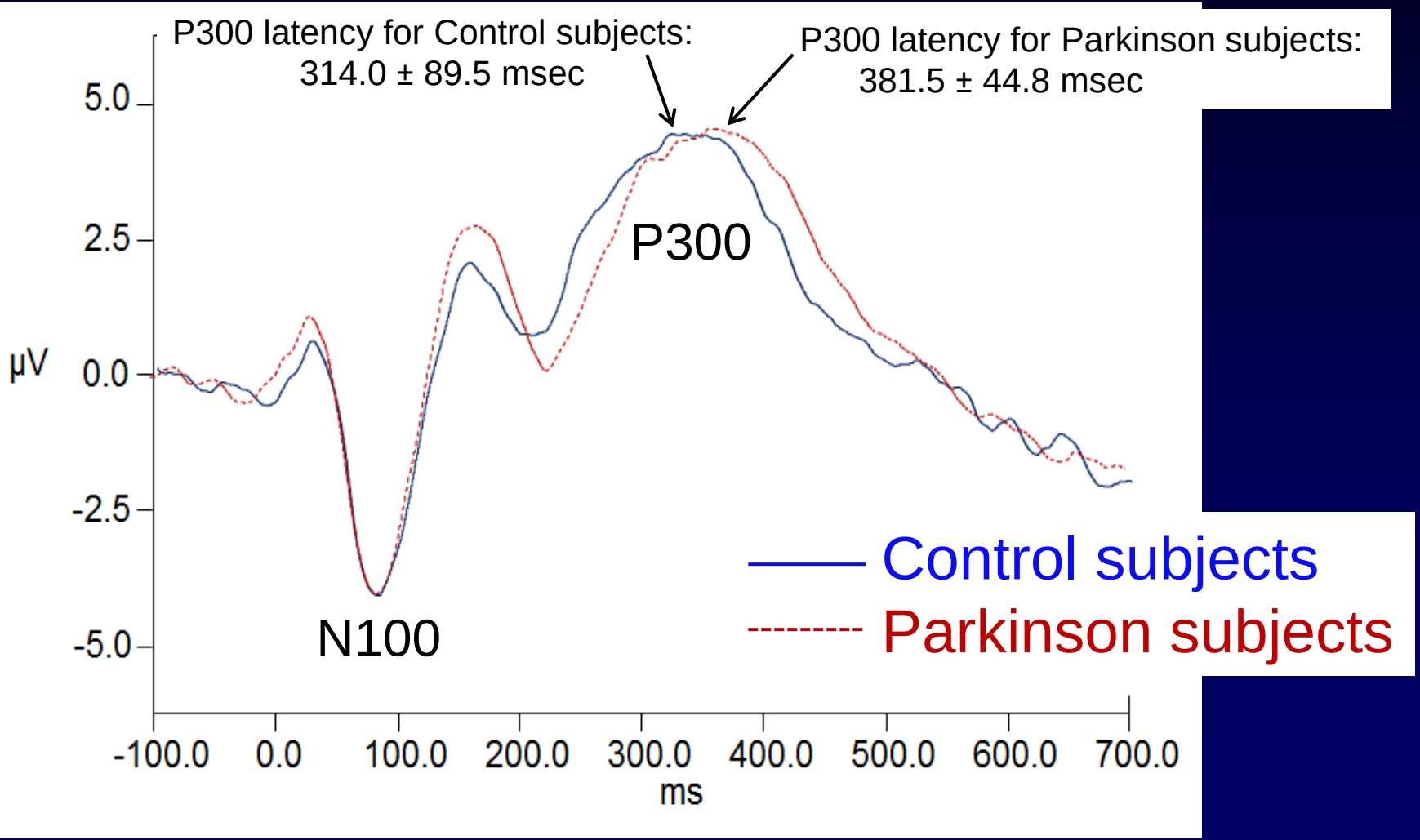
Auditory P300 Results

Responses to 500 Hz “frequent” **non-target** tones



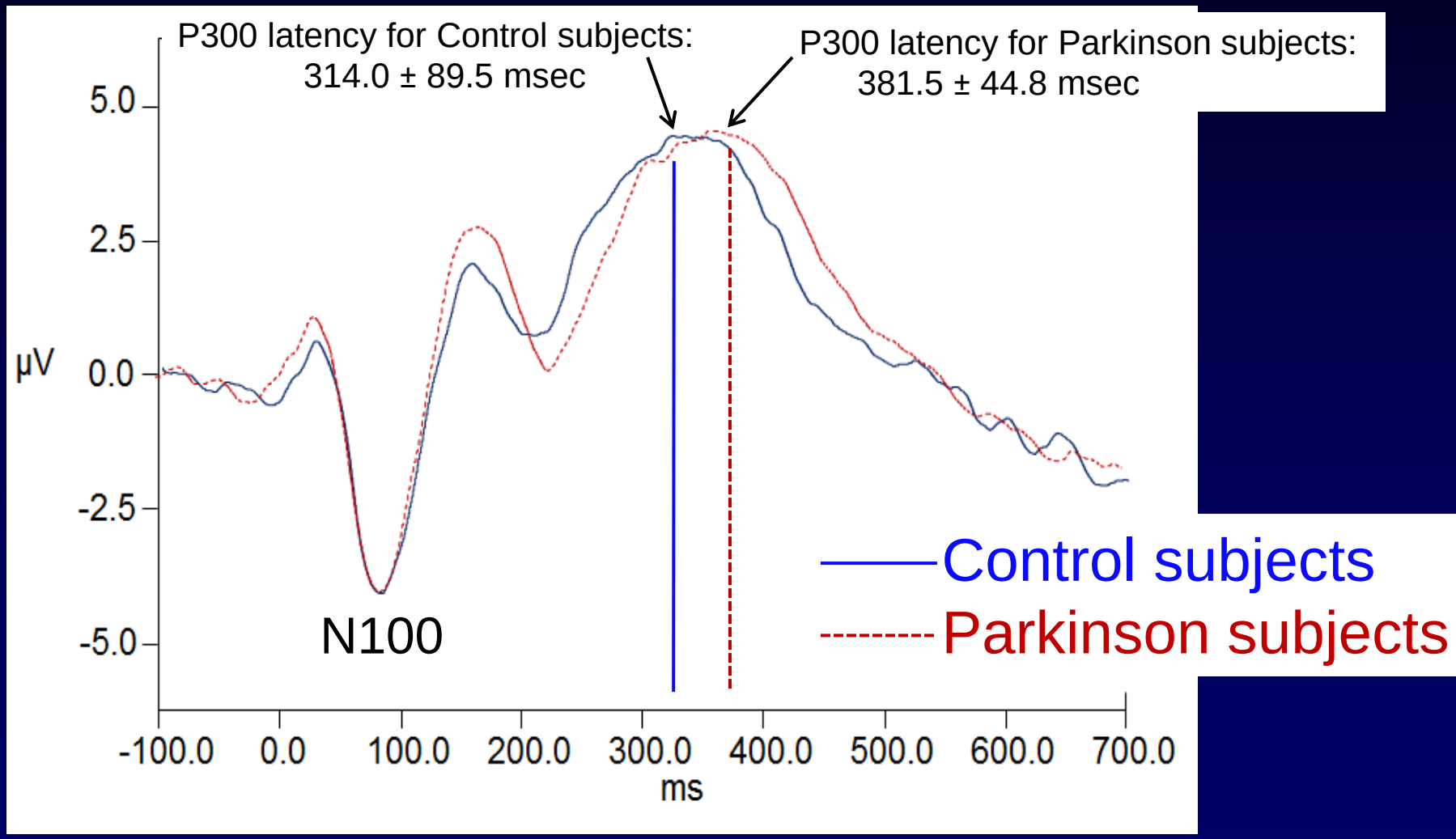
Auditory P300 Results

Responses to 1000 Hz “rare” **target** tones



Auditory P300 Results

Responses to 1000 Hz “rare” **target** tones



Electrophysiological Protocols

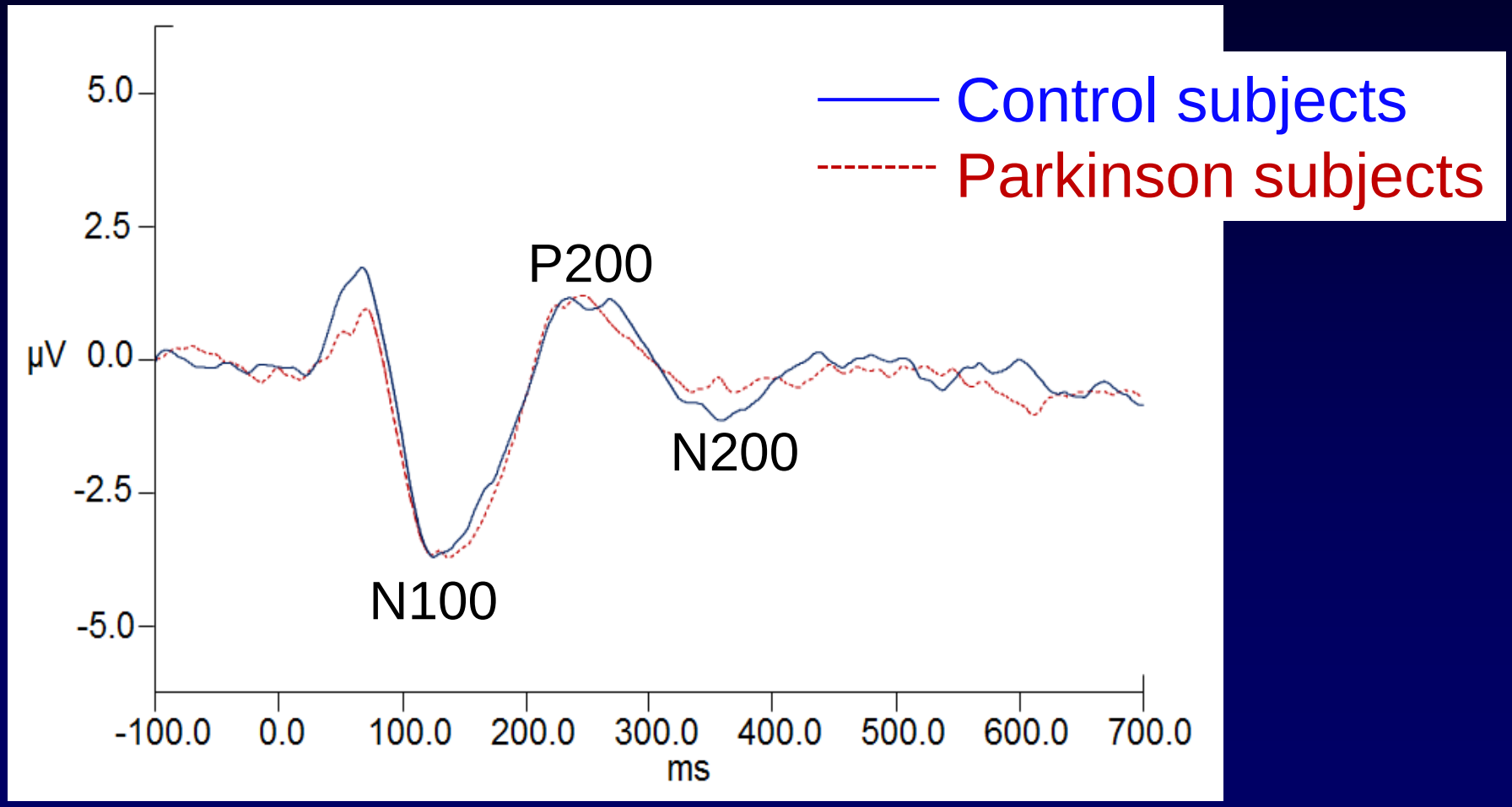
- Long-Latency Auditory Event-Related Potentials

Dichotic Digits protocol

Stimuli:	Spoken digits 1,2,3,4,5,6 85 dB SPL, ISI = 2.0 msec 150 (75%) non-target digits 1,2,3,5,6 50 (25%) target digit “4”
Presentation:	Binaural through insert earphones Two runs with target in R or L ears
Recording:	15 scalp electrodes Gain = 100,000 LF cutoff = 0.05 Hz HF cutoff = 100 Hz Rejection rate = 6 dB / octave
Subjects’ task:	Press a button when they hear the target digit (“4”) in either ear

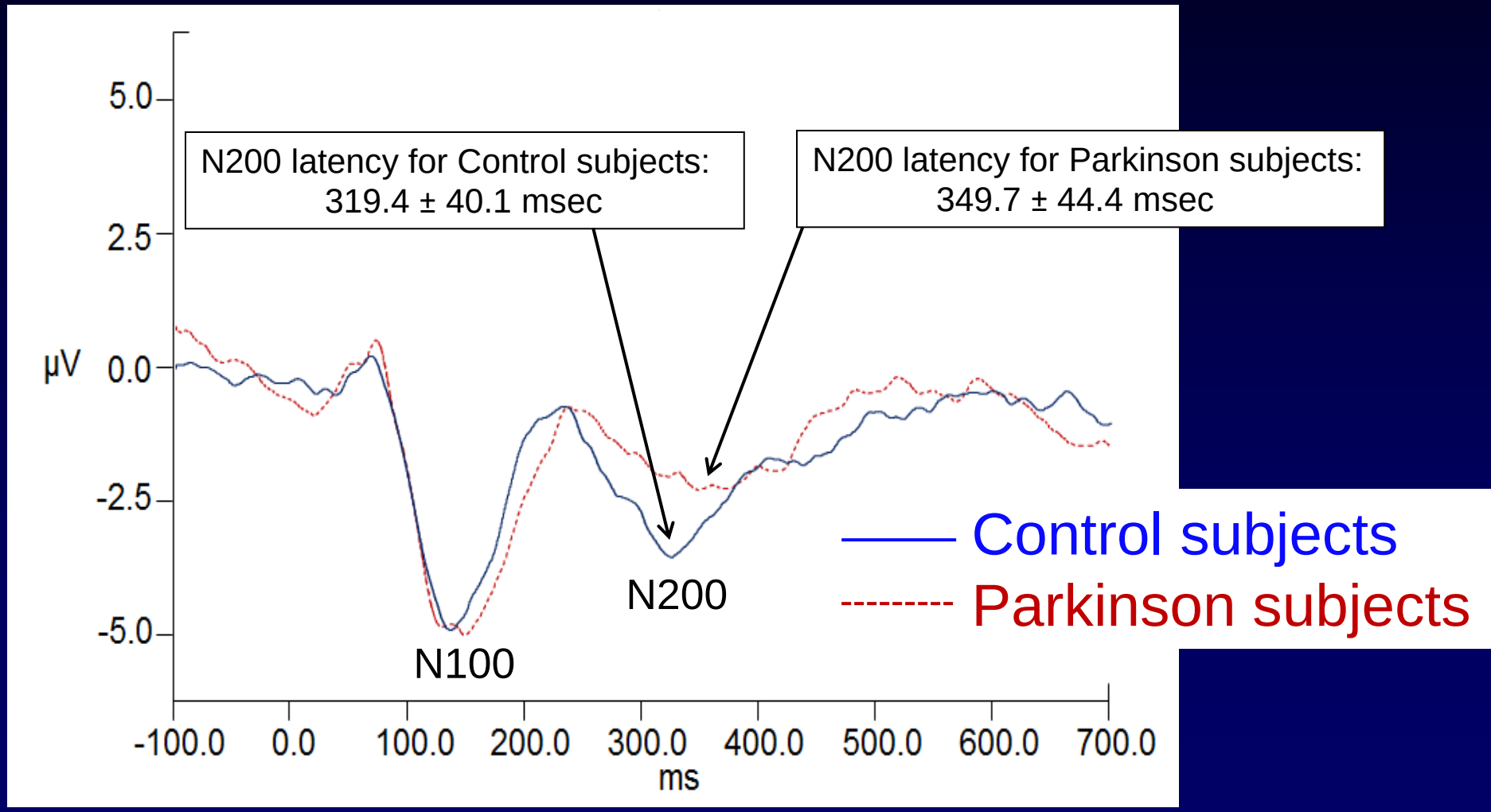
Dichotic Digits Results

Responses to **non-target** digits 1,2,3,5,6



Dichotic Digits Results

Responses to **target digit "4"**



LONG LATENCY AERP GENERATORS

WAVE	LATENCY (msec)	GENERATOR(S)
N100	75-140	Auditory Cortex
P200	150-230	Auditory Cortex, Sensory integration cortex
N200	200-350	Sensory integration cortex, Frontal cortex
P300	250-400	Reticulothalamus, Medial septal area*, Frontal cortex

*connects to hypothalamus, hippocampus, amygdala

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- Compared to Control Subjects, PD Patients had worse hearing at 1500 and 2000 Hz.
- No significant differences in neuropsychological results might reflect severity of PD and education levels exhibited by patients in this study.
- Worse performance on Spatial Release from Masking Test by PD patients compared to Controls.
- Compared to Control Subjects, PD Patients had delayed auditory P300 and N200 components.
  ⇨ might be an early indicator of cognitive decline

Summary of Findings from the Study

- 74% of PD patients admitted that they “often” or “sometimes” have difficulty hearing the words people are speaking

- 77% of PD patients are good candidates for amplification;
  however, only 26% of these candidates use hearing aids

- PD patients often have communication problems (speech and hearing)

Recommendations

- Because of the many physical, emotional and cognitive challenges that PD patients will face as their disease progresses, it is vital to identify and remediate auditory dysfunction in this population as early as possible.

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- It is important for PD patients to optimize communication with their family members, caregivers, friends, and clinicians, including pharmacists. Also, it is important for PD patients who develop hypophonia and other problems with speech production to be able to hear themselves and feedback from others (including speech pathologists) as clearly as possible.

Recommendations

- Get a hearing test
- If you are a candidate for hearing aids, try them

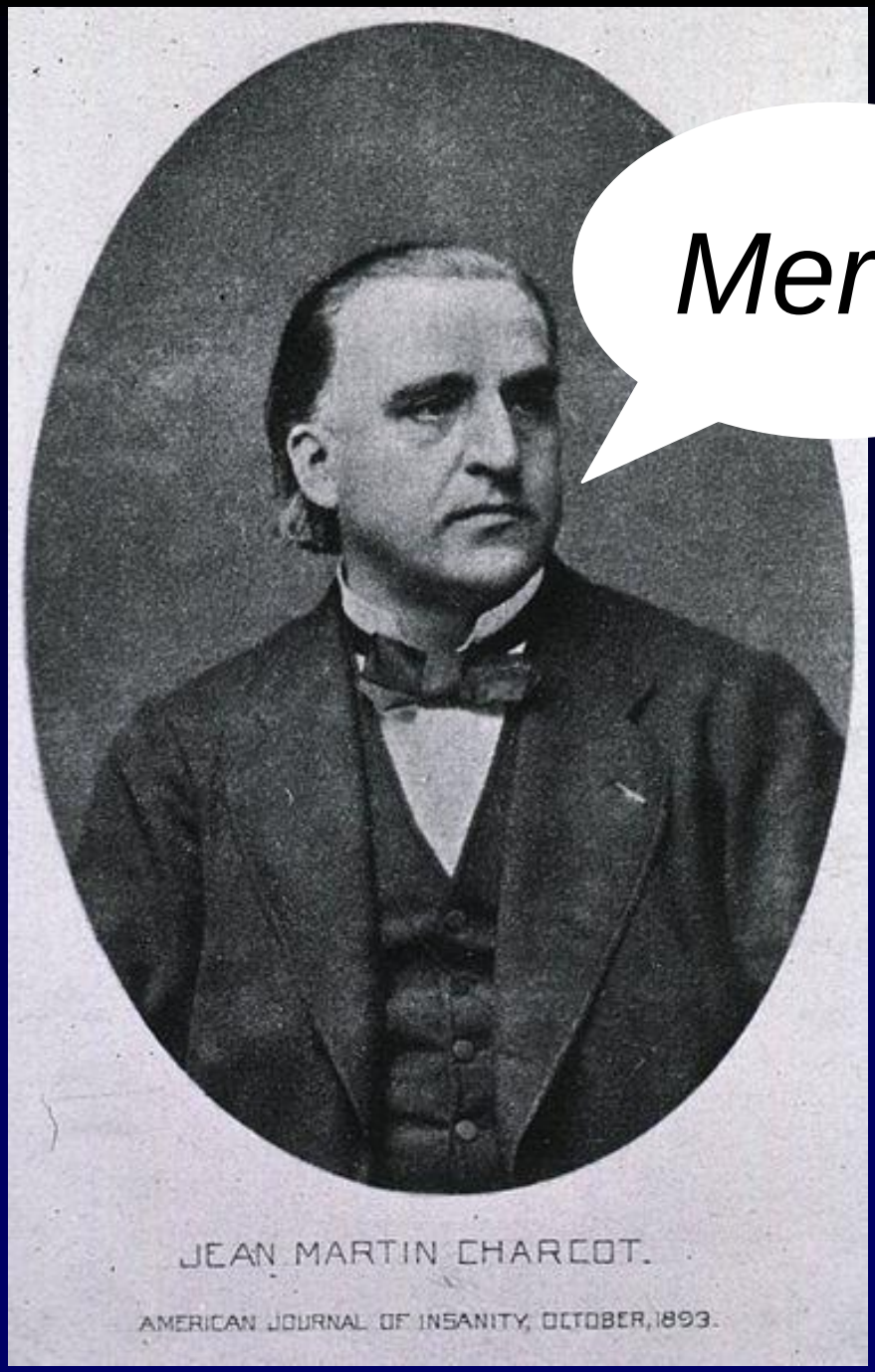
e.g., Phonak Lyric hearing aid is implanted in the ear canal – stays there for 3-4 months before it needs to be replaced

- Appropriate amplification can improve hearing ability, speech understanding, and sound localization and might also help to reduce the patient's risk or severity of cognitive decline, anxiety, and depression

Recommendations

- Assistive listening devices including amplified telephones, TV listening devices, and personal FM systems for use in public settings such as lectures, plays, or religious services. Also, visual alerting devices can increase awareness of alarms and doorbell rings.

- Employ communication optimization strategies, which include good environmental lighting, decreasing background noise, and encouraging speakers to do the following:
  (a) Speak at a reasonable rate.
  (b) Speak when their face can be seen clearly (keep their hands away from their face)
  (c) Get the listener's attention before speaking.
  (d) Speak to people from a reasonable distance (3–6 ft), not from a different room.


Merci!
JEAN MARTIN CHARCOT.
AMERICAN JOURNAL OF INSANITY, OCTOBER, 1893.