Auditory Function in Patients with Parkinson Disease

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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

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

<table>
<thead>
<tr>
<th></th>
<th>250 Hz</th>
<th>500 Hz</th>
<th>1,000 Hz</th>
<th>2,000 Hz</th>
<th>4,000 Hz</th>
<th>8,000 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 Parkinson patient (40 ears)</td>
<td>22.80 ± 10.97</td>
<td>19.37 ± 10.51</td>
<td>18.25 ± 12.01</td>
<td>27.75 ± 18.77</td>
<td>44.38 ± 21.49</td>
<td>60.75 ± 27.23</td>
</tr>
<tr>
<td>24 control group (48 ears)</td>
<td>19.37 ± 8.85</td>
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<td>16.98 ± 10.35</td>
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<td>32.19 ± 17.47</td>
<td>50.21 ± 22.19</td>
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<td><em>p</em></td>
<td>&gt;0.05</td>
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**Table 1** Comparison of pure tone audiometry threshold (dB) results (mean ± SD) at different frequencies for parkinsonian and control group

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Mean age of PD patients = 69.9 years
Mean age of control subjects = 63.8 years
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
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- Abnormal auditory P300s in PD patients reported by
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  - 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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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 at all 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
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
World Health Organization Disability Assessment Schedule (WHODAS II)

Total Score

PD Patients: 48.6 ± 11.8

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p = 0.0009
World Health Organization Disability Assessment Schedule (WHODAS II)

Total Score

PD Patients: $48.6 \pm 11.8$

Control Subjects: $38.7 \pm 10.3$

$p = 0.0009$

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?

<table>
<thead>
<tr>
<th></th>
<th>OFTEN</th>
<th>SOMETIMES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD PATIENTS</td>
<td>11 (31%)</td>
<td>15 (43%)</td>
<td>9 (26%)</td>
</tr>
<tr>
<td>CONTROL SUBJECTS</td>
<td>2 (6%)</td>
<td>24 (69%)</td>
<td>9 (26%)</td>
</tr>
</tbody>
</table>
### Hearing Handicap Inventory for Adults (HHIA)

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

**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
- 12% Severe Problem
- 32% Mild to Moderate
- 56% Little or No Problem

Control Subjects
- 6% Severe Problem
- 30% Mild to Moderate
- 64% Little or No 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

Control subjects

PD patients
Pure Tone Audiometric Results

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)
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)

- **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)

Four Test Conditions:
- Right non-competing (RNC)
- Right competing (RC)
- Left competing (LC)
- Left non-competing (LNC)
STAGGERED SPONDAIC WORD TEST (SSW)

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

<table>
<thead>
<tr>
<th></th>
<th>LEFT EAR GAP THRESHOLD</th>
<th>RIGHT EAR GAP THRESHOLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD PATIENTS</td>
<td>9.7 ± 3.4 msec</td>
<td>8.9 ± 3.5 msec</td>
</tr>
<tr>
<td>CONTROL SUBJECTS</td>
<td>8.9 ± 4.5 msec</td>
<td>8.7 ± 4.8 msec</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>LEFT EAR % CORRECT</th>
<th>RIGHT EAR % CORRECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD PATIENTS</td>
<td>86 ± 12%</td>
<td>93 ± 13%</td>
</tr>
<tr>
<td>CONTROL SUBJECTS</td>
<td>84 ± 13%</td>
<td>88 ± 14%</td>
</tr>
</tbody>
</table>

Normal outcome for this test is ≥ 90% correct for people with normal hearing or mild hearing loss.
Spatial Release from Masking (SRM) Test

Quiet

Position of Target Sentence

Co-located

Position of Masker Sentence

Separated

Position of Target Sentence

-45°/+45°
Ready Charlie go to red five now.

Ready Tiger go to green eight now.

Ready Ringo go to blue two now.

Quiet

Co-located 0°/0°

Separated -45°/+45°
Spatial Release from Masking (SRM) Test

SRM 0 Degrees (Co-Located Sentences)

p=0.059

Worse

Better

Controls

Parkinson
Spatial Release from Masking (SRM) Test

SRM 45 Degrees: Controls vs. Parkinson

p=0.002
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
Scalp electrodes connected to non-inverting inputs of differential preamplifiers

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

Graph showing P200 and N100 responses for control subjects and Parkinson subjects.
Auditory P300 Results

Responses to 1000 Hz “rare” target tones

P300 latency for Control subjects:
314.0 ± 89.5 msec

P300 latency for Parkinson subjects:
381.5 ± 44.8 msec
Auditory P300 Results

Responses to 1000 Hz “rare” target tones

P300 latency for Control subjects: $314.0 \pm 89.5$ msec

P300 latency for Parkinson subjects: $381.5 \pm 44.8$ msec

N100
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

- **Control subjects**
- **Parkinson subjects**
Dichotic Digits Results

Responses to target digit “4”

N200 latency for Control subjects: 319.4 ± 40.1 msec

N200 latency for Parkinson subjects: 349.7 ± 44.4 msec
## Long Latency AERP Generators

<table>
<thead>
<tr>
<th>Wave</th>
<th>Latency (msec)</th>
<th>Generator(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N100</td>
<td>75-140</td>
<td>Auditory Cortex</td>
</tr>
<tr>
<td>P200</td>
<td>150-230</td>
<td>Auditory Cortex, Sensory integration cortex</td>
</tr>
<tr>
<td>N200</td>
<td>200-350</td>
<td>Sensory integration cortex, Frontal cortex</td>
</tr>
<tr>
<td>P300</td>
<td>250-400</td>
<td>Reticulothalamus, Medial septal area*, Frontal cortex</td>
</tr>
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*connects to hypothalamus, hippocampus, amygdala
Summary of Findings from the Study

• Compared to Control Subjects, PD Patients had worse hearing at 1500 and 2000 Hz
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• No significant differences in neuropsychological results might reflect severity of PD and education levels exhibited by patients in this study.
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Summary of Findings from the Study

• 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. This 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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• 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.

• 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!