

# Audiological and Cognitive-Linguistic Manifestations in Rheumatic Disease

Susan Dillmuth-Miller Au.D., CCC-A

Associate Professor, Clinical Audiologist CSD

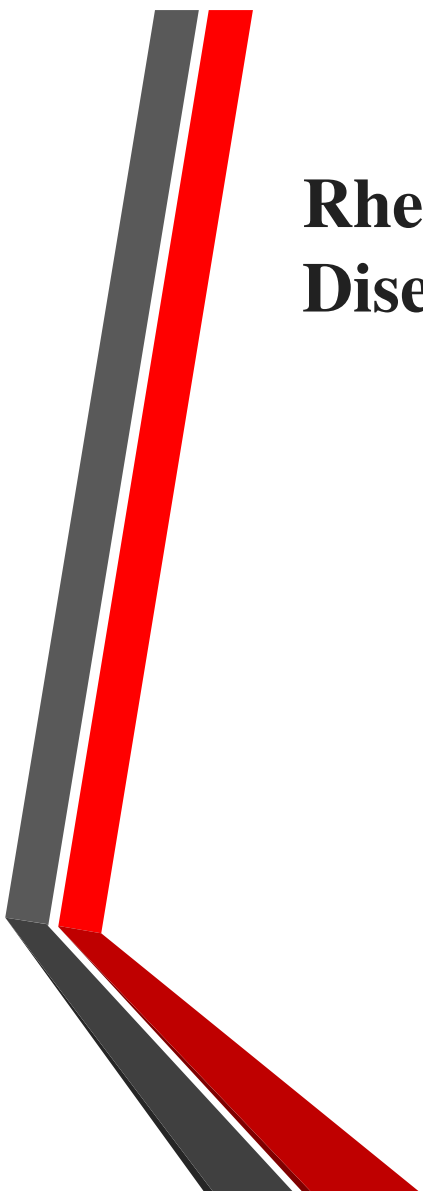
LuAnn Batson-Magnuson Ph.D., CCC-SLP

Associate Professor, Graduate Program Coordinator CSD

East Stroudsburg University

## Disclosures

- This research has been funded by Faculty Development and Research Grants sponsored by the Office of the Provost at East Stroudsburg University.
- Drs. Magnuson and Miller are employed by East Stroudsburg University (ESU) in the Department of Communication Sciences and Disorders. Drs. Magnuson and Miller have received compensation for a portion of their time spent on the project through the FDR Grant.
- Dr. Magnuson is diagnosed with rheumatoid arthritis and has relatives with varied rheumatic diseases.



## **Rheumatic Disease**

“Any of several diseases characterized by inflammation and pain in muscles or joints.”

# Extensive List of Rheumatic Diseases

- \* Ankylosing Spondylitis (AS)
- \* Arthritis
- \* Avascular Necrosis (Osteonecrosis) \ Back Pain
- \* Behçet's Disease
- \* Bursitis And Other Soft Tissue Diseases
- \* Carpal Tunnel Syndrome
- \* Chronic Fatigue Syndrome
- \* Collagen Vascular Disease
- \* CPDD (Calcium Pyrophosphate Dihydrate Crystal Deposition Disease )
- \* Crohn's Disease
- \* Degenerative Joint Disease
- \* Dermatomyositis
- \* DISH (Diffuse Idiopathic Skeletal Hypertosis)
- \* Dupuytren
- \* EDS (Ehlers-Danlos Syndrome)
- \* EMS (Eosinophilia-Myalgia Syndrome)
- \* Felty's Syndrome
- \* Fibromyalgia
- \* Fibromyositis
- \* Gout
- \* Infectious arthritis
- \* Inflammatory Bowel Disease
- \* JH (Joint Hypermobility)
- \* Joint Inflammation
- \* Juvenile Rheumatoid Arthritis
- \* Juvenile Arthritis - Other Types & Related Conditions
- \* Juvenile Dermatomyositis
- \* Juvenile Idiopathic Arthritis (JIA)
- \* Juvenile Non-Inflammatory Disorders
- \* Juvenile Psoriatic Arthritis
- \* Juvenile Rheumatoid Arthritis (JRA)
- \* Juvenile Scleroderma
- \* Juvenile Spondyloarthropathy Syndromes
- \* Juvenile Systemic Lupus Erythematosus (SLE)
- \* Juvenile Vasculitis
- \*  
Ledderhose Disease (Dupuytren of the feet)
- \* Lupus, Discoid
- \* Lupus Erythematosus
- \* Lyme Disease
- \* Marfan Syndrome
- \* MCTD (Mixed Connective Tissue Disease)
- \* Myofascial Pain
- \* Osteoarthritis
- \* Osteogenesis Imperfecta
- \* Osteonecrosis (Avascular Necrosis)
- \* Osteoporosis
- \* Paget's Disease
- \* Peyronie's Disease
- \* PMR (polymyalgia rheumatica)
- \* Polyarteritis Nodosa and Wegener's Granulomatosis
- \* Polyarthritits
- \* Polymyositis
- \* Pseudogout
- \* Pseudoxanthoma Elasticum (PXE)
- \* Psoriatic Arthritis
- \* Raynaud's
- \* Reiter's (Reactive Arthritis)
- \* Rheumatoid Arthritis
- \* RLD (Restless Leg Syndrome)
- \* RSD (Reflex Sympathetic Dystrophy)
- \* Sarcoidosis
- \* Scleroderma
- \* Sjögren's Syndrome
- \* Soft Tissue Disease
- \* Spinal Stenosis
- \* Still's Disease
- \* Temporal Arteritis
- \* TMJ (Temporo-Mandibular Joint) problems
- \* Undifferentiated Spondylarthropathy
- \* Wegener's Granulomatosis
- \* Vasculitis



## **Recognized Shared Characteristics of Rheumatic Diseases**

- Affect joints, tendons, ligaments, bones, and muscles
- Inflammation
- Patients experience:
  - Pain
  - Fatigue
- At increased risk of:
  - cardiovascular and cerebrovascular disease

## Evidence of an Inflammatory Process in the Brain

- Inflammation within the brain
  - Serum
  - EEG
  - MRI
  - PET
- Immune factors
- Premature cardiovascular disease- accelerated atherosclerosis

## Evidence of Inflammatory Process: Serum

- **High levels of antiphospholipid antibodies**<sup>(SLE)</sup>
  - persistently positive levels assoc. with cognitive decline
- **Higher concentration of S100B protein** (RA, SLE)
  - a marker of glial cell damage (RA)
- **High levels of CSF chemokine CX3CL1** (also known as fractalkine)
- **Release of inflammatory mediators** - cytokines, chemokines and prostaglandins<sup>(SLE, RA)</sup>
- **Mixed results of elevation of IL-8 in blood serum but consistently high CSF IL-8 levels** (Fibro)
- **Elevated levels of CCL-19 secreted protein involved in inflammatory process**– (Lyme) post-treatment Lyme Disease Syndrome less research available

## **Evidence of Inflammatory Process: EEG Evidence**

- **prolongation of P300 latency** (SLE)
  - indication possible demyelination
- **reduction of P300 amplitude** (SLE)
  - a neuro-physiological analogue for cognitive dysfunction



# Imaging Evidence of Inflammatory Process: MRI

- **Hypoperfusion**
  - **frontal lobe** (SLE, RA) (scleroderma)
  - **parietal lobe and temporal lobes** (RA)
- **Activation of glial cells** (SLE, RA)
- **White matter lesions** (SLE)
- **Ventricular dilation** (SLE)
- **Cortical atrophy** (SLE)
- **Myelinopathy** (SLE)
- **Decreases in thalami, the thalamocortical tracts, and both insular regions** (Fibro)
- **Decreases in gray matter volume in the postcentral gyri, amygdalae, hippocampi, superior frontal gyri, and anterior cingulate gyri** (Fibro)

# Imaging Evidence of Inflammatory Process

## PET Scan Evidence

- Bilateral parieto-occipital white matter hypometabolism (SLE)
- Problems with glucose metabolism (SLE)
  - (Found also in patients exhibiting pre-AD and TBI)

## SPECT Scan Evidence

- Abnormalities in perfusion to various areas of the brain (SLE)
  - most notably the frontal, temporal, and parietal lobes  
(Lyme)

# Types of Cognitive-Linguistic Deficits:

- **Deficits in memory:**
  - STM Recall of digits, words, sentences
  - Working and episodic memory
- **Sustained Attention Weaknesses**
- **Verbal Fluency deficits (phonemic and semantic)**
- **Slower cognitive response times, slower processing**
- **Executive Functioning Deficits**
- **Deficits in verbal reasoning and comprehension**
- **Mathematical processing**



## **Impact of Language and Cognitive Deficits**


- Cognitive deficits result in early retirement
- Reduced QOL

The majority of patients do not receive therapy for these deficits!

# Rheumatoid Arthritis



[This Photo](#) by Unknown Author is licensed under [CC BY-NC](#)



**Current  
Study RA  
Group:  
Subject  
Description**

- Total number of research subjects = 21
- 17 females and 4 males with a mean age of 51.9 years
- Education- some college or completed college

## Current Study RA Group: Conclusion

### Word-finding (TAWF)

- **53%** of subjects with RA fell **below age-expected** performance levels
- Performance on word finding task was not related to level of disease activity, pain, sleepiness or emotional state at time of testing

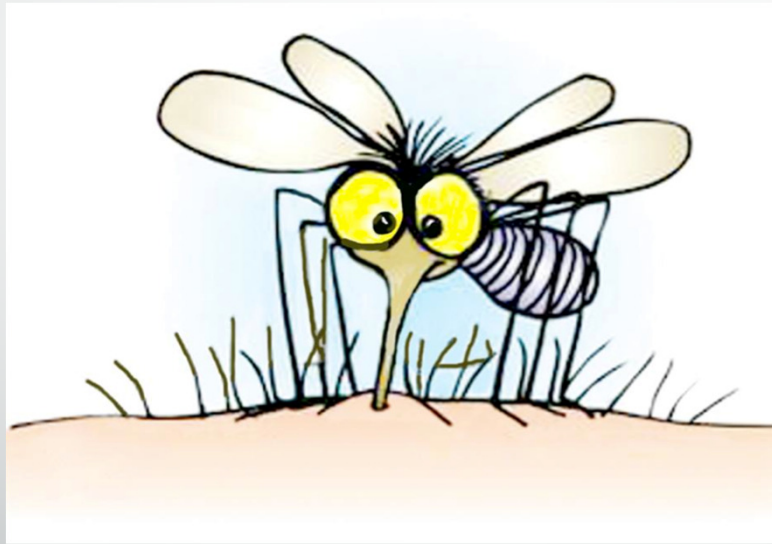
### Executive Functioning (FAVRE)

- **27%** of subject with RA fell **below age-expected** performance levels for accuracy of responses
- **67%** of subject with RA fell **below age-expected** performance levels for providing rationale
- **7%** of subject with RA fell **below age-expected** performance levels for the time of task completion
- A relationship was not found between verbal reasoning and executive functioning (accuracy, timing, or rationale) and emotional state, pain level, sleepiness, or disease activity at the time of testing

### Memory (RBMT 3)

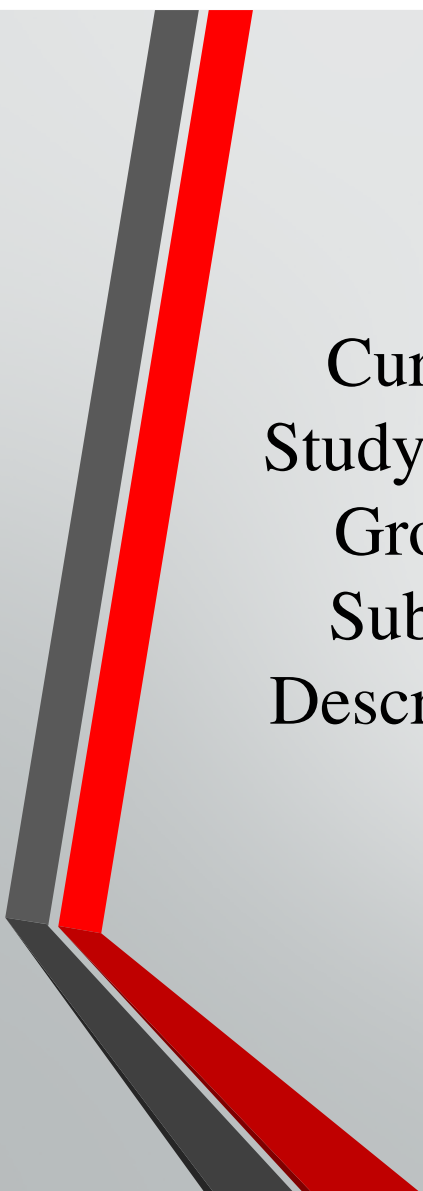
- **40%** of subjects fell **at or below 25% tile** age-expected performance levels

# Lyme Disease



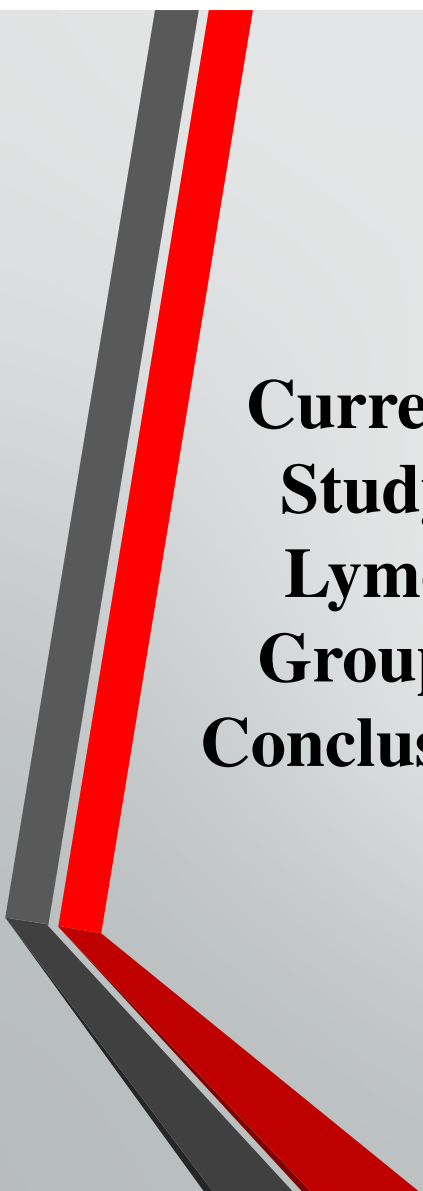
[This Photo](#) by Unknown Author is licensed under [CC BY-NC-ND](#)





Current  
Study Lyme  
Group:  
Subject  
Description

- Total number of research subjects = 6
- 6 females and 0 males with a mean age of 37.1 years
- Education- some college or completed college



**Current  
Study  
Lyme  
Group:  
Conclusion**

**Word-finding (TAWF-2)**

- **33%** fell **below age-expected** performance levels
- not related to level of disease activity, pain, sleepiness or emotional state at time of testing

**Executive Functioning (FAVRE)**

- **33%** fell **below age-expected** performance levels for accuracy
- **50%** fell **below age-expected** performance for rationale
- **0%** fell **below age-expected** performance levels for time

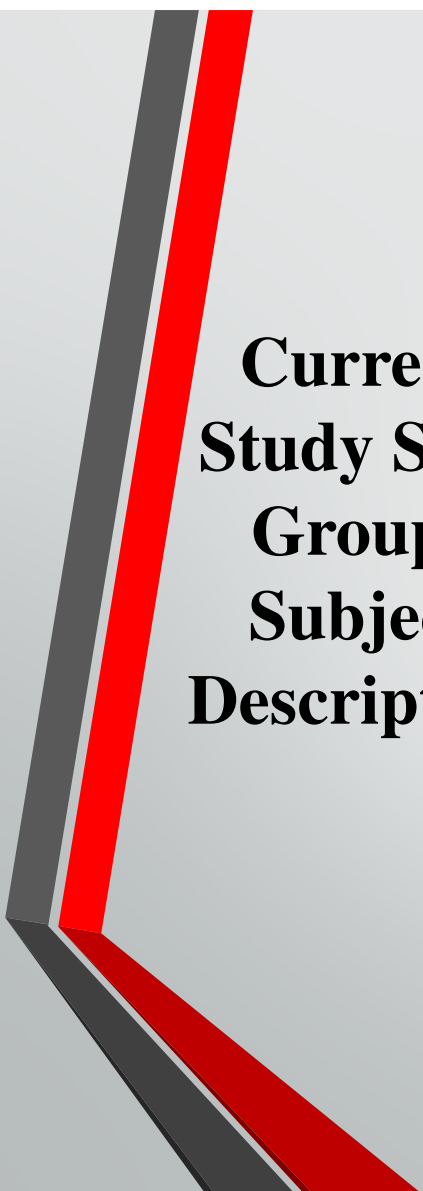
**Memory (RBMT 3)**

- **50%** subjects scored **below age-expected** levels
- No correlation between pain, sleepiness, emotional state or disease activity
- RBMT-3 subtest performance: Delayed tasks were more difficult

# Systemic Lupus Erythematosus

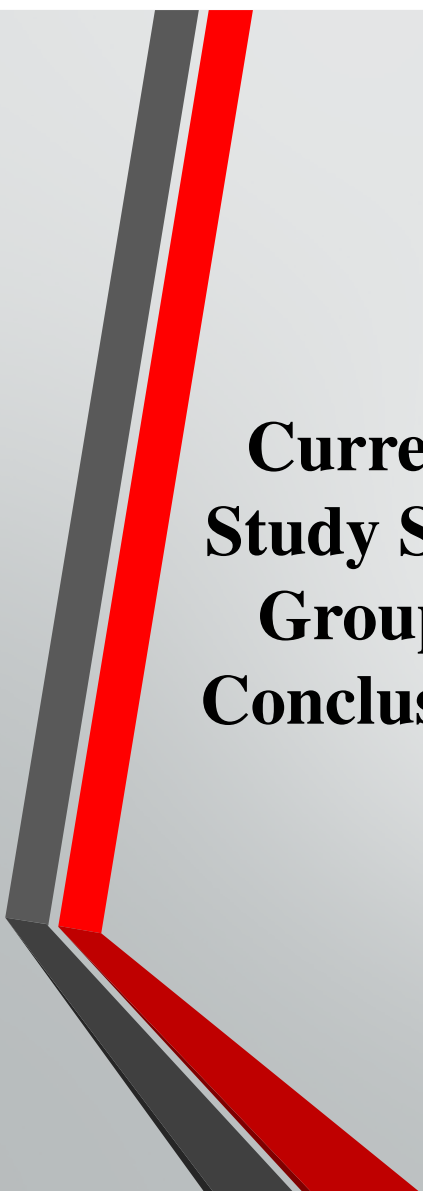


[This Photo](#) by Unknown Author is licensed under [CC BY](#)



**Current  
Study SLE  
Group:  
Subject  
Description**

- Total number of research subjects = 5
- 5 females and 0 males with a mean age of 36.6 years
- Education- some college or completed college



## Current Study SLE Group: Conclusion

### Word-finding (TAWF-2)


- **40%** fell **below age-expected** performance levels
- Performance not related to level of disease activity, pain, sleepiness or emotional state at time of testing

### Executive Functioning (FAVRE)

- **60%** fell **below age-expected** performance levels for accuracy of responses
- **40%** fell **below age-expected** performance for rationale
- **40%** fell **below age-expected** performance levels for time

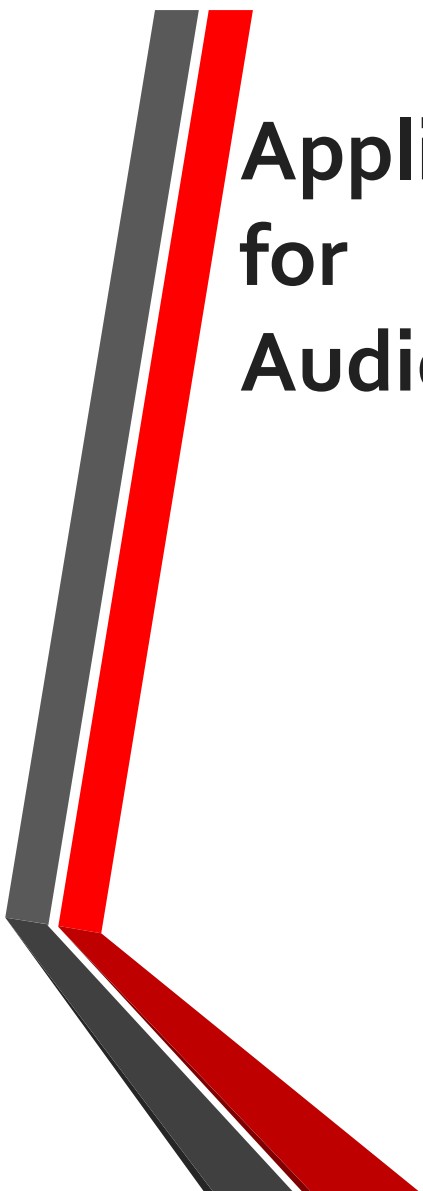
### Memory (RBMT-3)

- **40%** subjects scored **below age-expected** levels
- No correlation between pain, sleepiness, emotional state or disease activity
- RBMT-3 subtest performance: Delayed tasks were more difficult



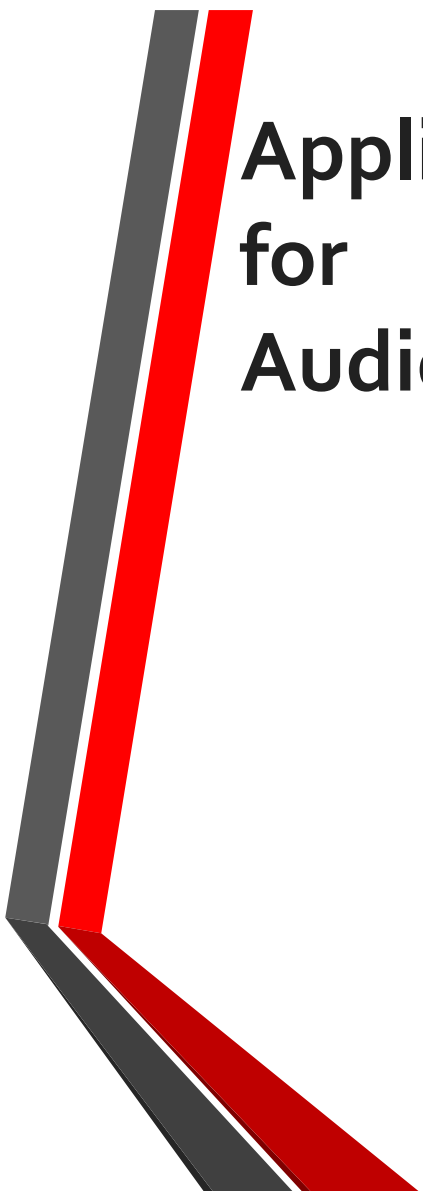
## **Current Study: Cognitive- Linguistic Conclusions**

- Clients with RA, Lyme disease and SLE present with deficits in memory, executive functioning and word finding to varying degrees and with varying patterns.
- RA and Lyme Disease: No significant interactions were noted between pain, sleepiness, and disease activity on any of the cognitive test outcomes



## Application for Audiologists

- . Is the client's performance impacted by inaccurate responses? (STM memory/working memory?)
- . Is the client's performance impacted by the rate of presentation? (word finding/word fluency or slowed processing?)
- . Is it appropriate to pause and provide wait time for a response?



## Application for Audiologists

- Consider the impact word-finding deficits and slowed processing particularly delayed response times on APD testing
- Consider the impact of short term memory deficits on APD testing
- **Refer to a speech-language pathologist:**
  - Assessment of linguistic memory and word-finding prior to APD testing



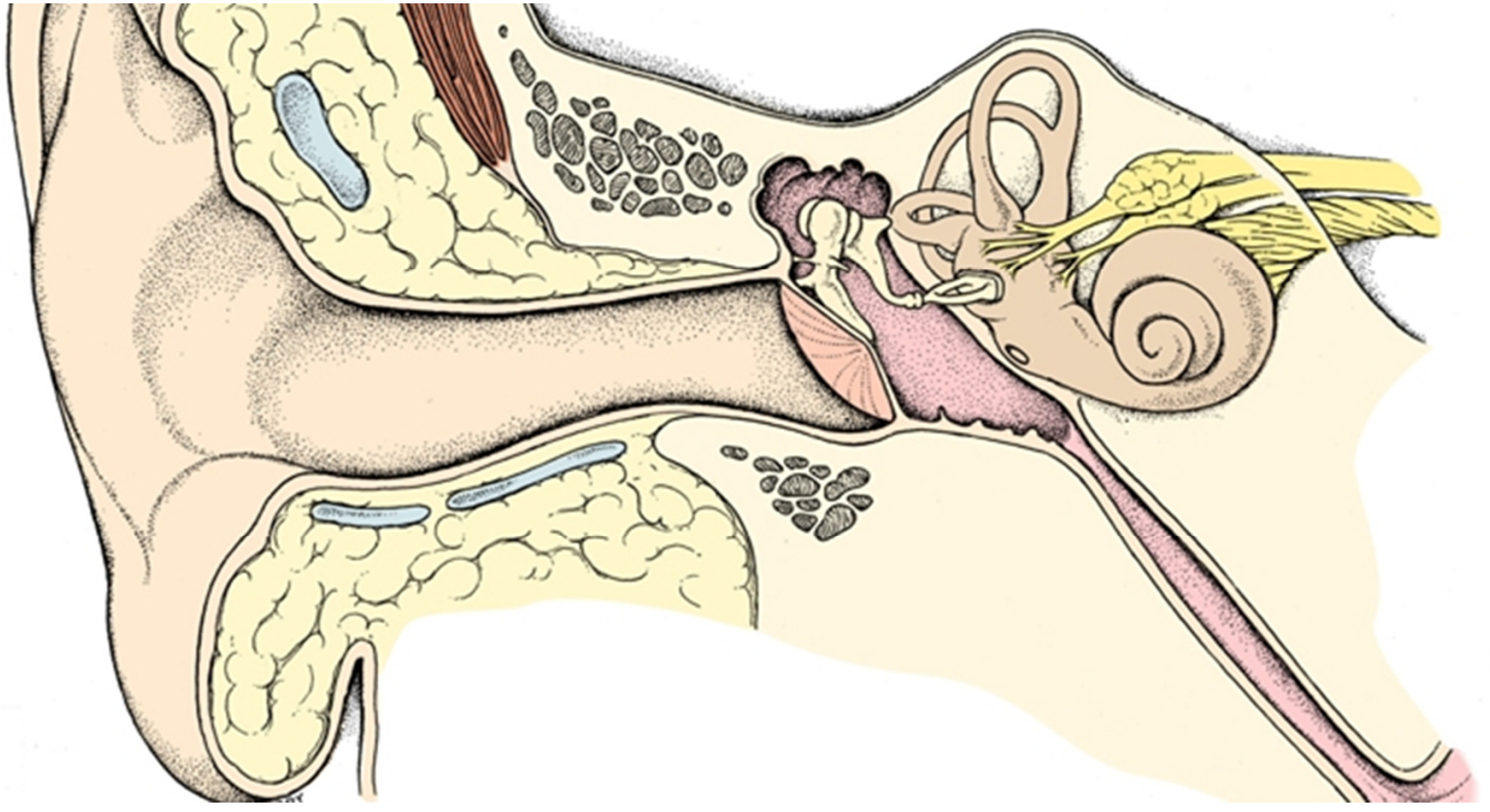


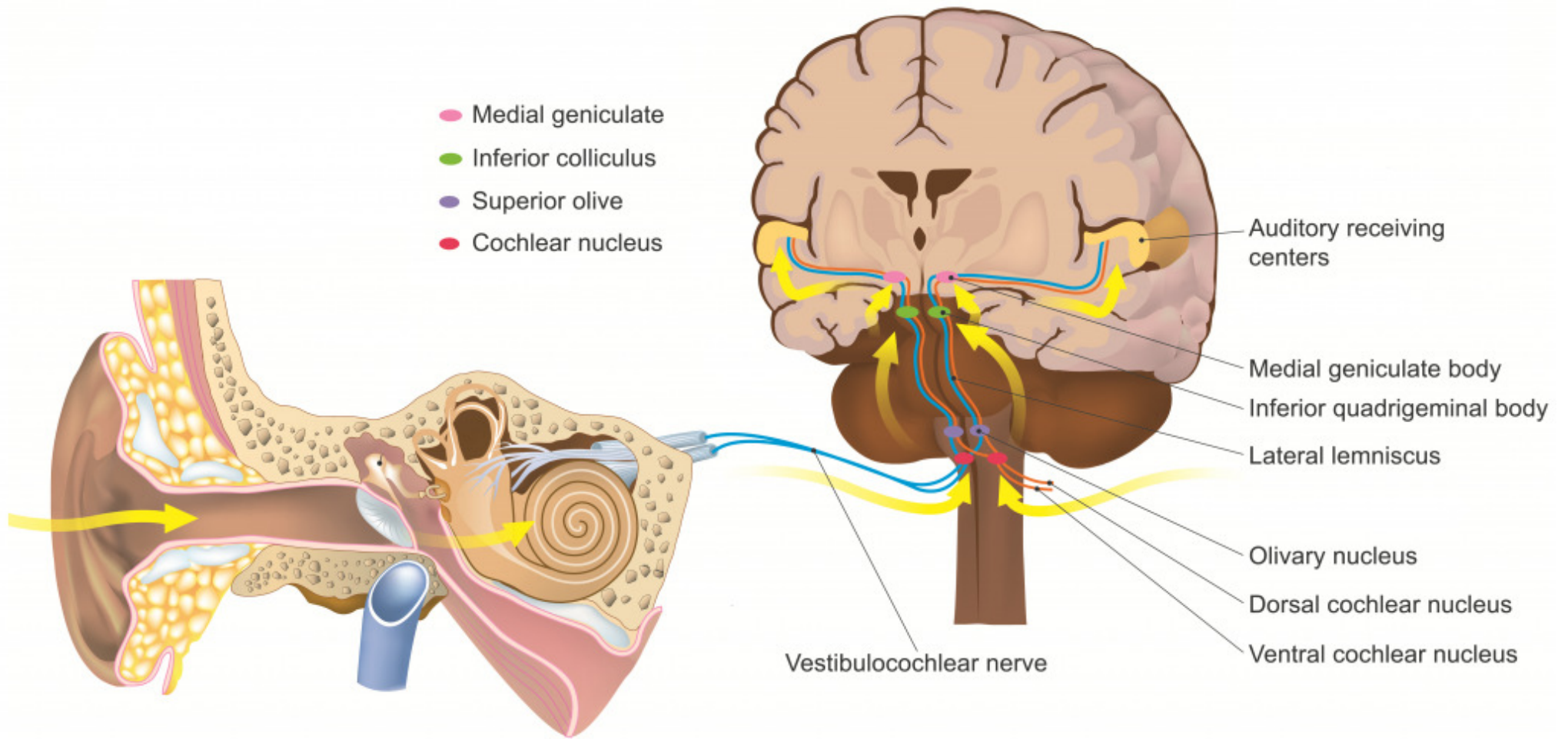
## **Future Directions**

- . Assess the impact of latent response times on repeated/modeled information typical of APD testing
- . Correlational Analysis between Cognitive-Linguistic Test Results and Audiological Findings



# **Audiological Manifestations**





<https://teachmeanatomy.info/wp-content/uploads/The-Cochlear-Nucleus-of-the-Auditory-Pathway-1024x493.png>



## **Reasons for Variability in Studies**

- Some studies used subjective report
- Some studies did not conduct Bone Conduction
- Studies varied in number of subjects
- A screening substituted as an evaluation
- Hearing Loss defined differently.
- Use of age-matched controls


# Audiological Manifestations

## RA

- Incidence of HL 24-89%
- Mostly bilateral SNHL
  - Conductive Hearing Loss possible but less common
- Related to length of disease with significant number developing HL during the first year
- Younger patients had thresholds worse than expected for age
- Flare ups- Bilateral fluctuating SNHL common

## SLE

- Incidence of HL
- Mostly bilateral SNHL
- Younger patients had decreased HF thresholds and older patients had decreased LF thresholds when compared to age-matched peers
- Associated with APD dysfunction-temporal problems
- Flare ups- unilateral fluctuating HL, sudden HL



## **Audiological Manifestations Fibromyalgia**

- 50% report otologic symptoms without audiolologically-detectable disease
- Asymptomatic high-frequency threshold reduction
- Middle-ear dysfunction not observed (n=67)
- Report hypersensitivity to sound
- Variety of ABR abnormalities which suggests APD

# Audiological Manifestations Lyme Disease

- Rare unilateral sensorineural hearing loss (single case study)
- 5/5 children with chronic LD were found to have mild to moderate auditory processing deficits
- 48% with Lyme-induced hyperacusis (with acoustic reflexes)
- 2% unresponsive to treatment with antibiotics





## Goals of the Current Study

- Assess performance in
  - Audiological Performance
    - Middle ear Status
    - Acuity
    - Auditory Processing
- Determine areas for further assessment in future studies
- Determine test protocols to identify deficits



## **Inclusionary/Exclusionary Criteria**

- Diagnosis of rheumatic disease
- No hx. of concussion or other brain injury
- No history of significant noise exposure
- Adult 18 or older
- No active middle ear disease
- No congenital hearing loss

# Types of Data

Data	Collected Via
Background Information	Questionnaire
HHIA-S	Questionnaire - <a href="#">link</a>
Hearing Evaluation	Dr. Miller
Auditory Processing Screening	Dr. Miller, Graduate Students



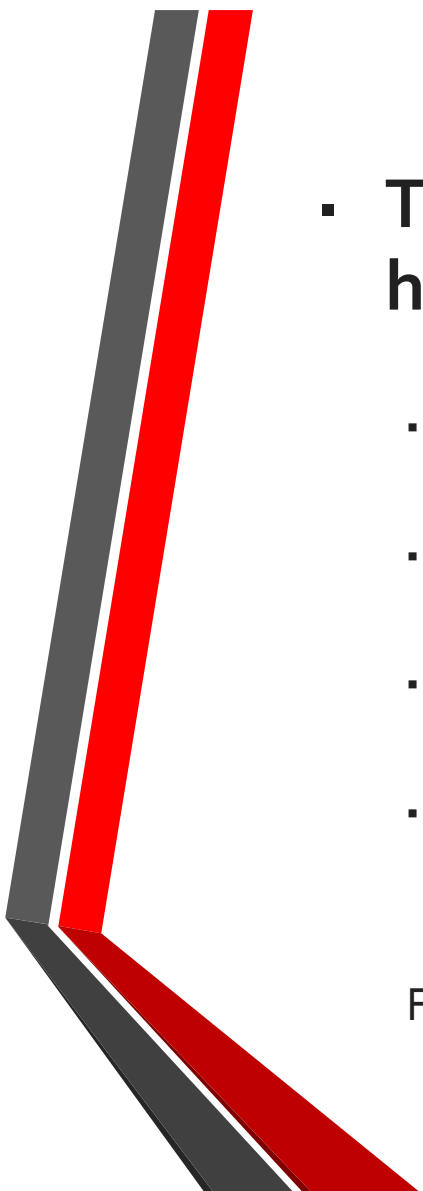
# Testing Protocol

- Otoscopy
- Tympanometry
- Ipsilateral and Contralateral Acoustic Reflexes
- Pure tone audiometry- AC and BC with interoctaves > 1k
- SRT's and Word Recognition at 40 dB SL using CID-W22- recorded stimuli.
- Distortion Product Otoacoustic Emissions (DPOAE) at 65/55 from 1.5k to 8k Hz.
- APD Screening (SCAN 3) if hearing levels symmetrical and better than 25 dB from 1-4k Hz.

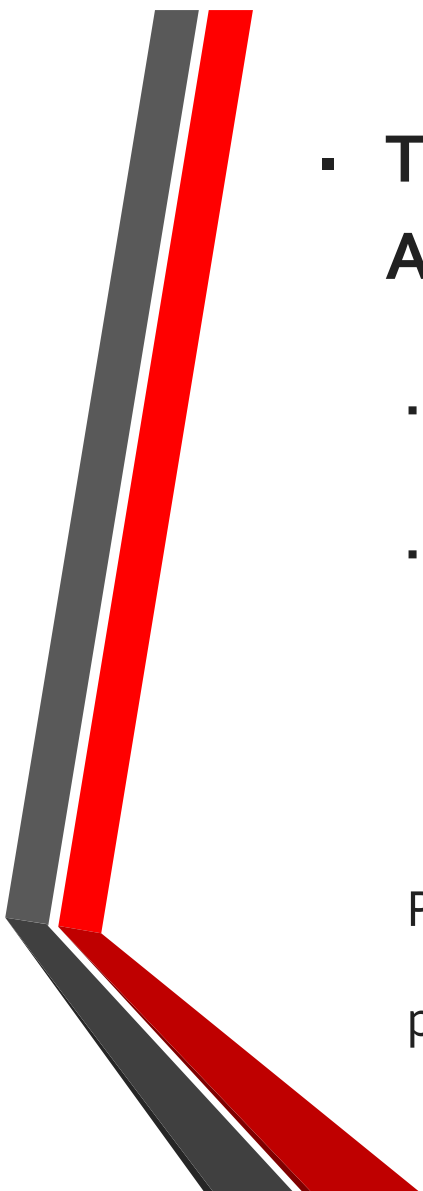


# Subjects

- 35 Subjects (all females)
  - Average age= 45.1 years
  - Age Range 20-76
  - **Diagnoses:**
    - RA = 16
    - Lupus = 5
    - Fibro = 8
    - Lyme = 6

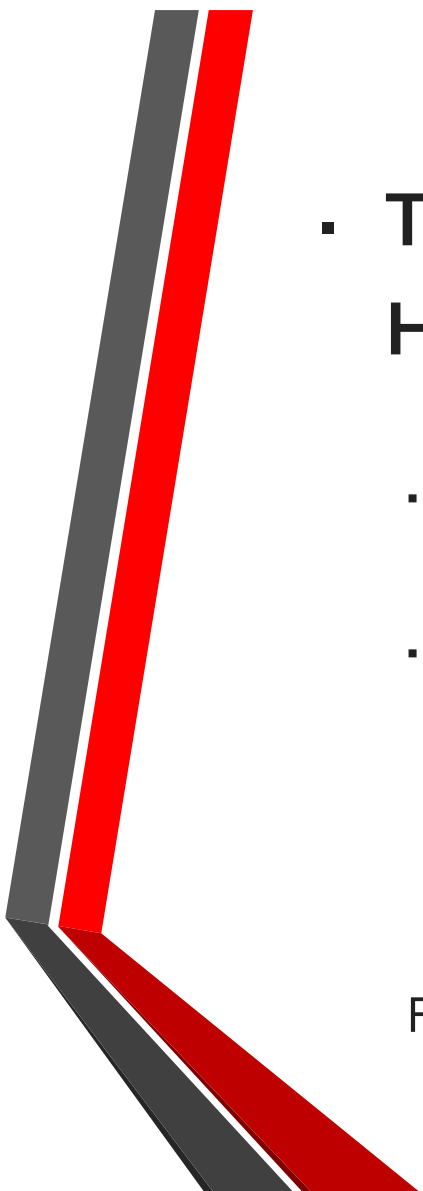
- 
- **There was no correlation between medications and hearing loss.**
    - Prednisone (p= .708)
    - NSAIDS (p=.486)
    - Methotrexate (p=.782)
    - Hydroxychloroquine (Plaquenil) (p=.527)

Fisher exact test with the level of significance  $p < .05$ .

- 
- **There was no correlation between the following and APD screening results:**
    - Epworth Sleepiness Scale (ESS) (p=.430)
    - Routine Assessment of Patient Index Data 3 (RAPID-3) (p=.589)

Pearson correlation with the level of significance

p< .05. (N= 34)

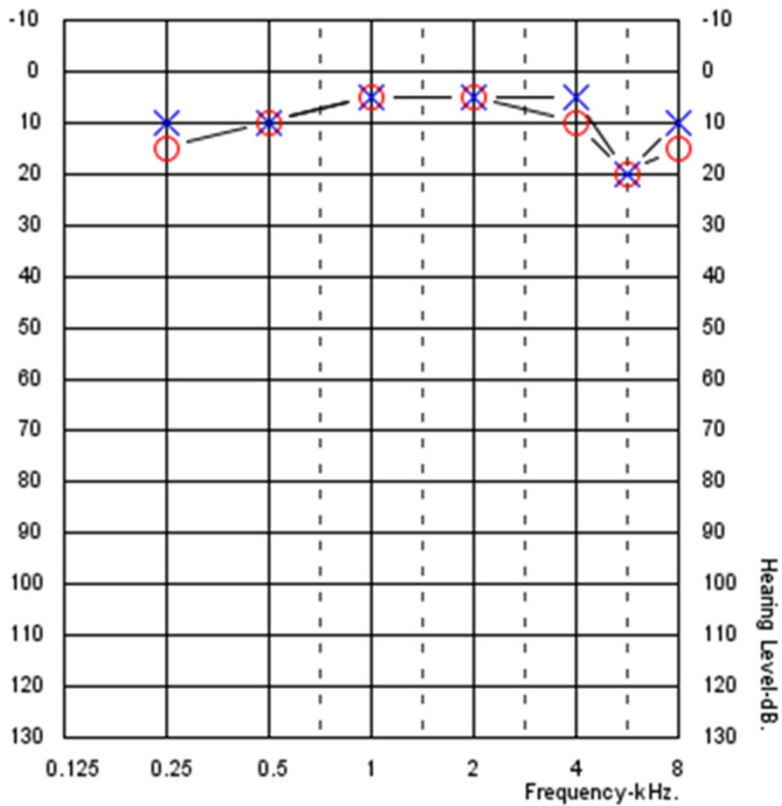
- 
- **There was no correlation between the Hearing Handicap Inventory for Adults and**
    - Hearing Loss (N=34,  $p=..546$ )
    - APD Screener Results (N=24,  $p=.671$ )

Fisher's Exact Test with the level of significance  $p < .05$ .

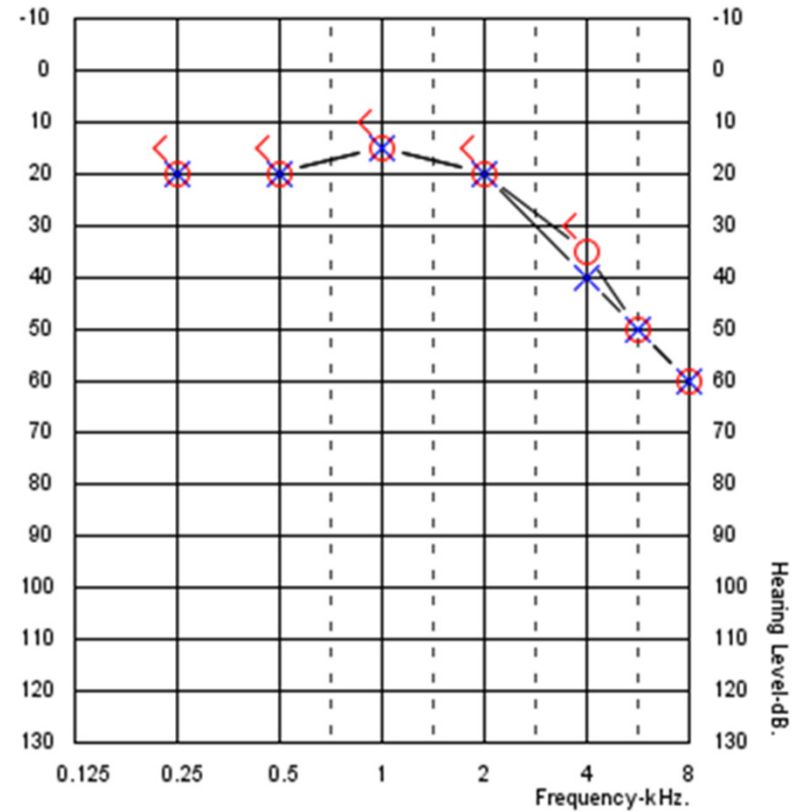


# All Groups

N=21, 18-60 yrs.  
PTA= 5.6 dB HL



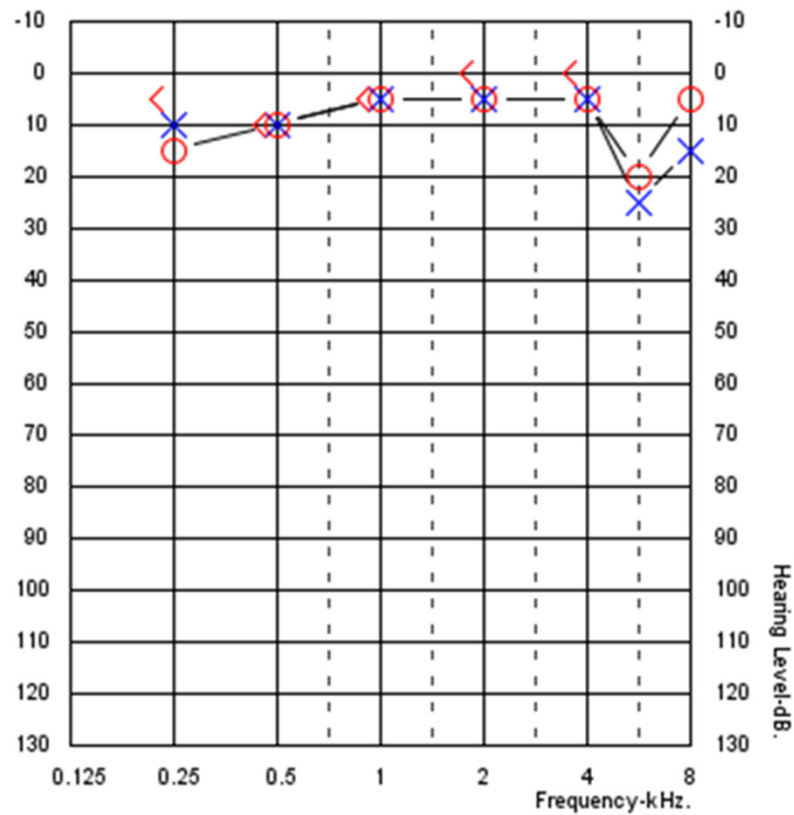
N=4, 61+ yrs.  
PTA= 21.7 dB HL



# Rheumatoid Arthritis

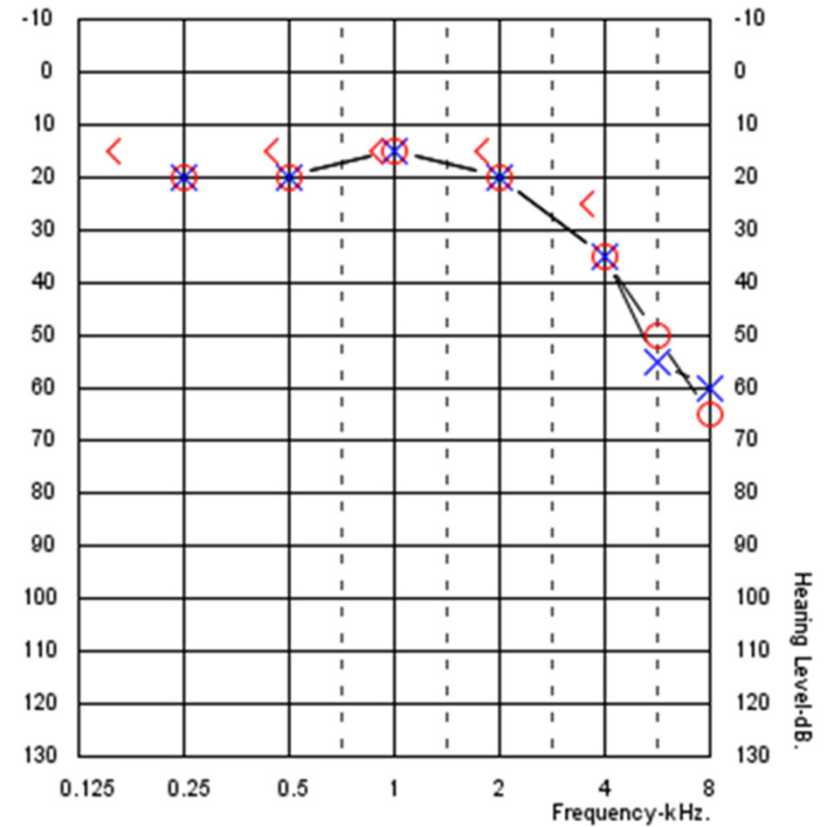
N=10, 18-60 yrs.

PTA= 4.5 dB HL x age= 42.7



N=4, 60 +

PTA= 21.7 dB HL, x age= 73





# Rheumatoid Arthritis

- 16 participants (not all had a hearing test)
- **16/16, 100%** reported vertigo and fluctuating hearing loss post diagnosis
- 13/14 had High frequency, SNHL
  - 9/10 in persons under 60
  - 4/4 in persons over 60
- 8/10 had 6000 Hz notch
- 1/14 had Type Ad tympanograms with no conductive component
- 4/10 did not pass APD screener
- OAE's absent above 4k Hz in those with at least a mild loss
- AR reflexes mostly present .5-4k in persons with mild to moderate hearing loss.

# Systemic Lupus Erythematosus (SLE)

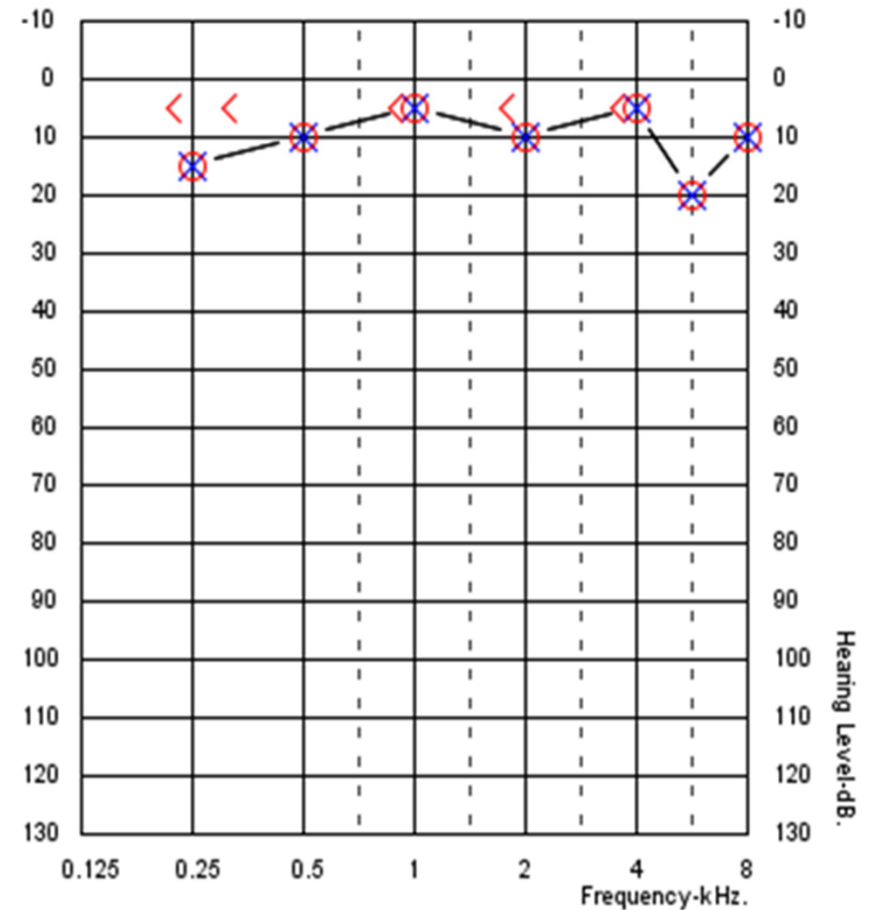
N=5, 18-60 yrs.  
average age= 34.8

PTA= 6.67 dB HL

All Subjects:

- \*had a 6k Hz notch
- \*had Type A tympanograms
- \*failed APD screener

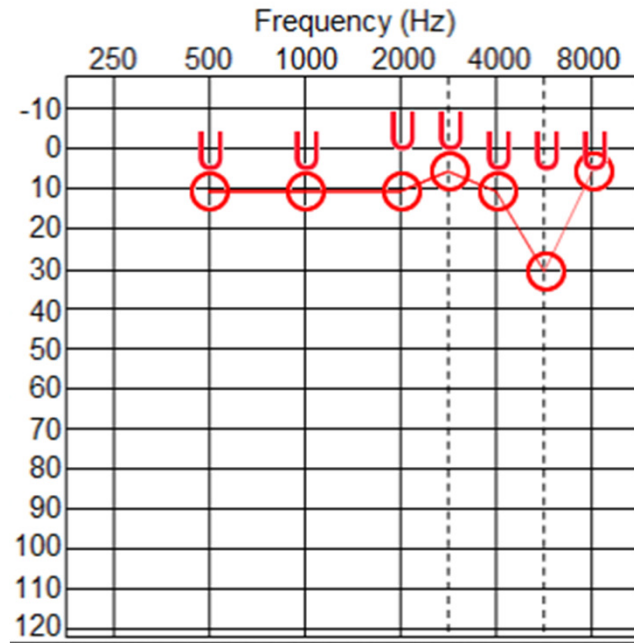
4/5 had sensorineural hearing loss  
1/5 had a conductive component)



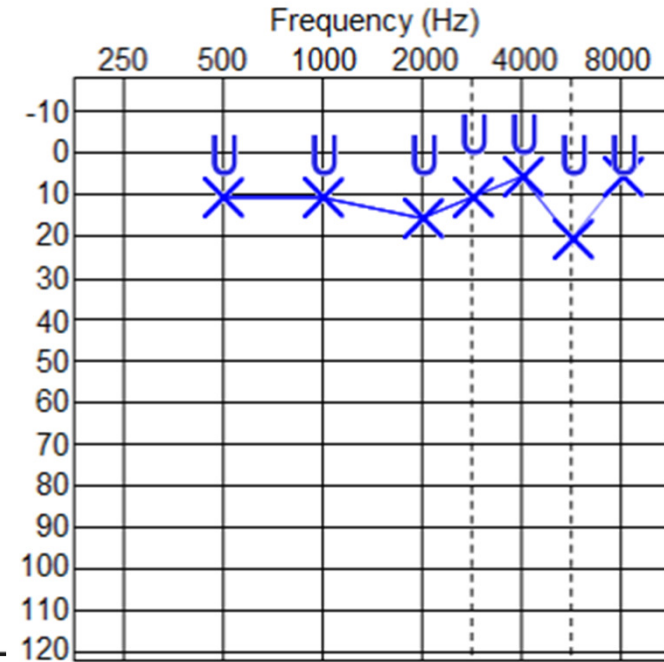
# SLE

## Case #172

- Female
- 24 years of age
- Diagnosed at 16 years of age
  
- 6K Hz notch bilaterally
- Mild Sensorineural HL
  
- HHIA-S – Did not Pass
- APD Screener- Did not Pass



Right ear  
U = control  
○ = right ear

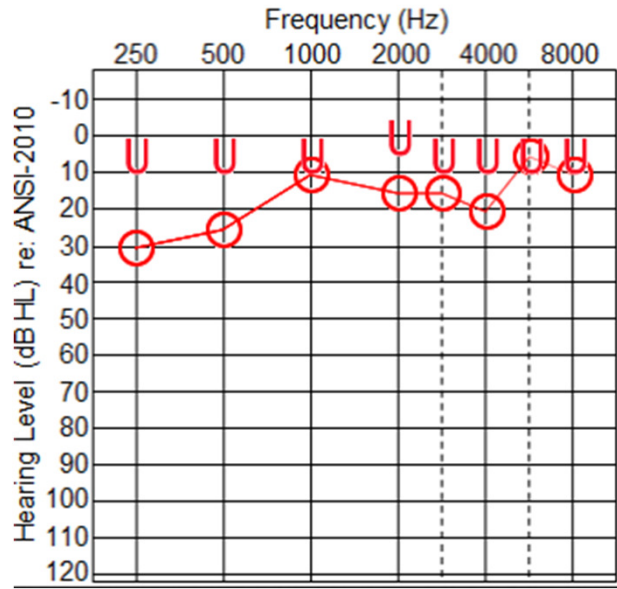


Left ear  
U = control  
X = Left ear

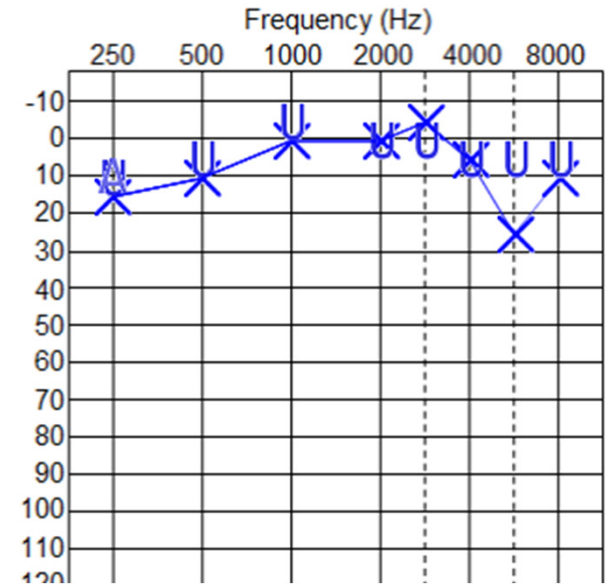
# SLE

## Case #132

- Female
- 44 years of age
- Diagnosed at 29 years
  
- 6K Hz notch in left ear
- LF conductive loss in right ear (Hx of OME)
- Mild Sensorineural HL
  
- HHIA-S: PASS
- APD Screener: Did Not PASS



Right ear  
U = control  
O = right ear



Left ear  
U = control  
X = Left ear

# Fibromyalgia

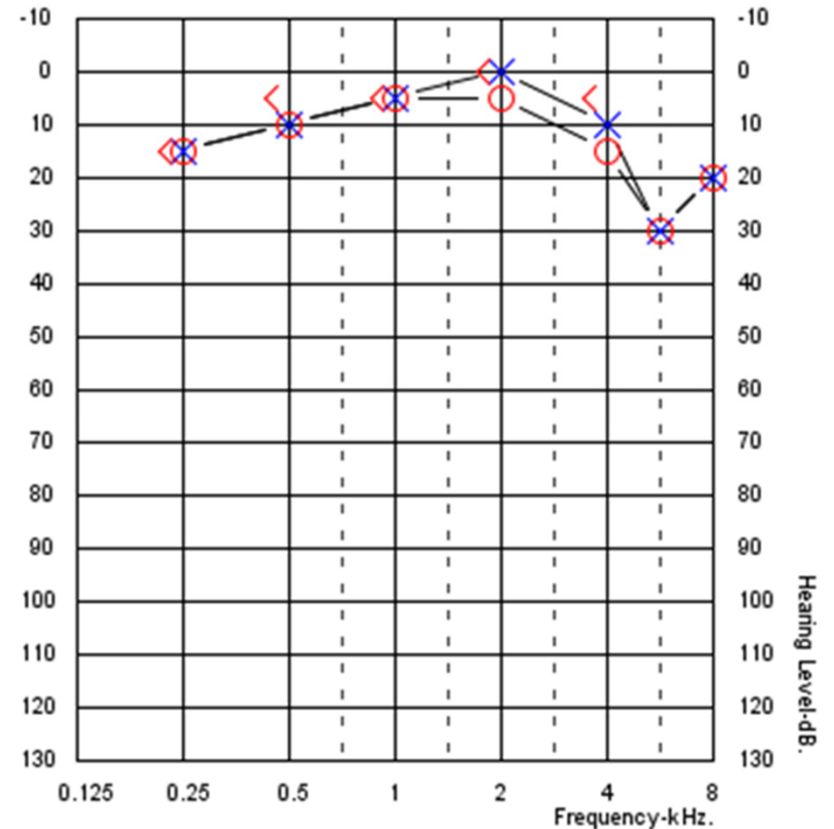
N=4, 18-60 yrs.  
average age= 37

PTA= 6.60 dB HL

All Subjects:

- \*had a 6k Hz notch and HL
- \*had Type A tympanograms
- \*failed APD screener

8/8 report tinnitus, vertigo, sensitivity  
to sound



# Lyme

7 participants

N=4, 18-60 yrs.  
average age= 37

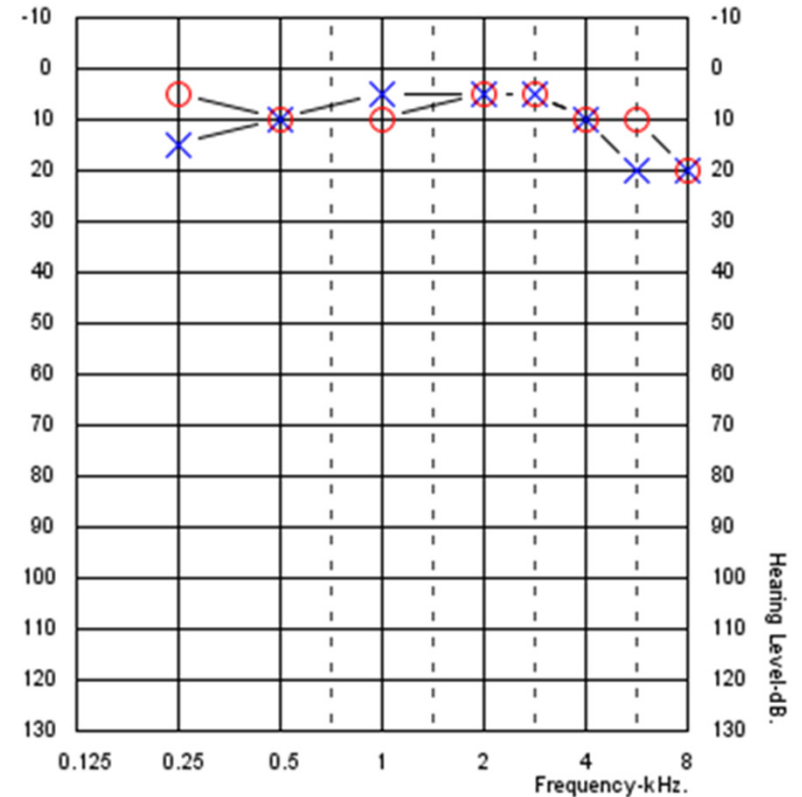
PTA= 5.42 dB HL

2/4 had high frequency hearing loss  
3/4 had 6k HL notch

All Subjects:

\*had Type A tympanograms

\*failed APD screener- CW







# Summary

- 21/25 had a 6k Hz notch (below 60) or sloping loss (60+)
- 17/17 did not pass APD screener.
  - Lyme primary deficit in competing words and other diagnoses had varied results
- Tympanograms were Type A and expected acoustic reflex pattern. (except for 2 persons with OME history).
- Hearing loss or APD not correlated with medications, sleepiness, or disease activity.



## **Study Limitations**

- Subject Numbers
- Multiple Diagnoses



**Why does it matter?**



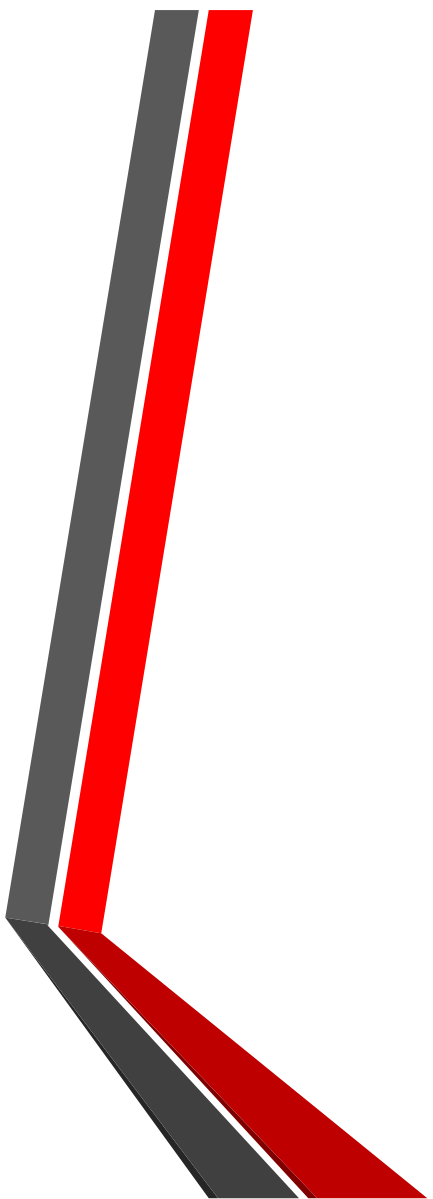
# Application to Audiologists

- Case History- Add questions about rheumatoid conditions
- All individuals with rheumatic conditions should have a full hearing evaluation shortly after diagnosis.
- Hearing levels should be monitored throughout the course of the disease.
- Including interoctaves
- APD screening/evaluation if hearing levels allow
- Refer those with rheumatic disease to a speech pathologist



## **Future Directions**

- Age and gender-matched controls
- Auditory physiology markers
- APD evaluations for those not passing screener
- Treatment effectiveness for APD



**Questions?**

# References

- Adhikari, T., Piatti, a., & Luggen, M. (2011). Cognitive dysfunction in SLE: development of a screening tool. *Lupus*, 20, 1142–1146. doi:10.1177/0961203311405374
- Andonopoulos, A. P., Naxakis, S., Goumas, P., & Lygatsikas, C. (1995). Sensorineural hearing disorders in systemic lupus erthematosus. A controlled study. *Clinical and Experimental Rheumatology*, 13, 137–141.
- Antin-Ozerkis, D., Evans, J., Rubinowitz, A., Homer, R. J., & Matthay, R. A. (2010). Pulmonary manifestations of rheumatoid arthritis. *Clinics in Chest Medicine*, 31(3), 451–78. doi:10.1016/j.ccm.2010.04.003
- Barr, W., Rastogi, R., Ravdin, L., & Hilton, E. (1999). Relations among indexes of memory disturbance and depression in patients with Lyme Borreliosis. *Applied Neuropsychology*, 6(1), 12-18. [http://doi.org/10.1207/s15324826an0601\\_2](http://doi.org/10.1207/s15324826an0601_2)
- Bartolini, M., Candela, M., Brugni, M., Catena, L., Mari, F., Fomonio, G., et al. (2002). Are behavior and motor performances of rheumatoid arthritis patiens influenced by subclinical cognitive impairments? A clinical and neuroimaging study. *Clinical and Experimental Rheumatology*, 20, 339-43.
- Batson-Magnuson, L., Dillmuth-Miller, S., Doll, E. 2018. Cognitive Linguistic Correlates in Rheumatic Disease. Unpublished raw data.
- Batson-Magnuson, L. (2015, November) Seminar on the Cognitive-Linguistic Correlates of Rheumatoid Arthritis and Systemic Lupus Erythematosus. Presented at the American Speech-Language-Hearing Association National Convention in Denver, CO.

# References

- Batuecas-Caletri, A., del Pino-Montes, J., Cordero-Civantos, C., Calle-Cabanillas, M. A., Lopez-Escamez, J. A. (2013). Hearing and vestibular disorders in patients with systemic lupus erythematosus. *Lupus*, 22, 437-442.
- Bowman, C. a, Linthicum, F. H., Nelson, R. a, Mikami, K., & Quismorio, F. (1986). Sensorineural hearing loss associated with systemic lupus erythematosus. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 94(2), 197-204.
- Bruner, A. P., Sato, E. I., & Pereira, L. D. (2009). Central auditory processing in patients with systemic lupus erythematosus. *Acta Reumatol Port*, 34(4), 600-607. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/20852573>
- Calderón, J., Flores, P., Babul, M., Aguirre, J., Slachevsky, a, Padilla, O., ... Massardo, L. (2014). Systemic lupus erythematosus impairs memory cognitive tests not affected by depression. *Lupus*, 1042-1053. doi:10.1177/0961203314536247
- Chen, Y.-M., Chen, H.-H., Lan, J.-L., & Chen, D.-Y. (2010). Improvement of cognition, a potential benefit of anti-TNF therapy in elderly patients with rheumatoid arthritis. *Joint, Bone, Spine : Revue Du Rhumatisme*, 77(4), 366-7. doi:10.1016/j.jbspin.2010.01.017
- Chi, A. C. (2010). Oral manifestations of systemic disease. *American Family Physician*, 82, 1381-88.



# References

- Coín-Mejías, M. A., Peralta-Ramírez, M. I., Santiago-Ramajo, S., Morente-Soto, G., Ortego-Centeno, N., Rubio, J.-L. C., ... Pérez-García, M. (2008). Alterations in episodic memory in patients with systemic lupus erythematosus. *Archives of Clinical Neuropsychology : The Official Journal of the National Academy of Neuropsychologists*, 23(2), 157–64. doi:10.1016/j.acn.2007.11.001
- Cutolo, M., Kitas, G. D., & van Riel, P. L. C. M. (2014). Burden of disease in treated rheumatoid arthritis patients: going beyond the joint. *Seminars in Arthritis and Rheumatism*, 43(4), 479–88. doi:10.1016/j.semarthrit.2013.08.004
- Denburg, S. D., Carbotte, R. M., & Denburg, J. A. (1997). Cognition and mood in systemic lupus erythematosus: Evaluation and pathogenesis. *Annals of the New York Academy of Sciences*, 823(905), 44–59. doi:10.1111/j.1749-6632.1997.tb48378.x
- Dikici, O., Muluk, N. B., Tosun, A. K., & Ünlüsoy, I. (2009). Subjective audiological tests and transient evoked otoacoustic emissions in patients with rheumatoid arthritis: Analysis of the factors affecting hearing levels. *European Archives of Oto-Rhino-Laryngology*, 266(11), 1719–1726. <https://doi.org/10.1007/s00405-009-0975-y>
- Geterud Å, Bake B, Bjelle A, Jonsson R, Sandberg N, & Ejnell H. (1991). Swallowing problems in rheumatoid arthritis. *Acta Otolaryngol (Stockh)*, 111, 1153-1161.
- Gimeno, D., Marmot, M. G., & Singh-Manoux, A. (2008). Inflammatory markers and cognitive function in middle-aged adults: The Whitehall II study. *Psychoneuroendocrinology*, 33, 1322–1334. doi:10.1016/j.psyneuen.2008.07.006

# References

- Gow, P.J. & Gibson, T. (1977). Dysphagia due to vertical subluxation of the axis in rheumatoid arthritis. *Rheumatology and Rehabilitation*, 16(3), 155-157  
doi:10.1093/rheumatology/16.3.155
- Halligan, C. S., Bauch, C. D., Brey, R. H., Achenbach, S. J., Bamlet, W. R., McDonald, T. J., & Matteson, E. L. (2006). Hearing loss in rheumatoid arthritis. *The Laryngoscope*, 116 (November), 2044–2049. doi:10.1097/01.mlg.0000241365.54017.32
- Hanly, J. G., Omisade, A., Su, L., Farewell, V., & Fisk, J. D. (2010). Assessment of cognitive function in systemic lupus erythematosus, rheumatoid arthritis, and multiple sclerosis by computerized neuropsychological tests. *Arthritis and Rheumatism*, 62(5), 1478–1486. doi:10.1002/art.27404
- Holliday, S. L., Navarrete, M. G., Hermosillo-Romo, D., Valdez, C. R., Saklad, a R., Escalante, a, & Brey, R. L. (2003). Validating a computerized neuropsychological test battery for mixed ethnic lupus patients. *Lupus*, 12, 697–703. doi:10.1191/0961203303lu442oa
- Kamen, D. L., & Strange, C. (2010). Pulmonary manifestations of systemic lupus erythematosus. *Clinics in Chest Medicine*, 31(3), 479–488.  
doi:10.1016/j.ccm.2010.05.001
- Kaplan, R. F., Meadows, M. C., Vincent, L. L., Logigian, E., & Steere, A. (1992). Memory impairment and depression in patients with Lyme encephalopathy: Comparison with fibromyalgia and nonpsychotically depressed patients. *Neurology*, 42(7), 1263-1267.  
<http://doi.org/10.1212/WNL.42.7.1263>
- Kaplan, R., Jones-Woodward, L., Workman, K., Steere, A., Logigian, E., & Meadows, M. (1999). Neuropsychological deficits in Lyme disease patients with and without other evidence of central nervous system pathology. *Applied Neuropsychology*, 6(1), 3-11.[http://doi.org/10.1207/s15324826an0601\\_1](http://doi.org/10.1207/s15324826an0601_1)
- Karatas, E., Onat, A. M., Durucu, C., Baglam, T., Kanlikama, M., Altunoren, O., & Buyukhatipoglu, H. (2007). Audiovestibular disturbance in patients with systemic lupus erythematosus. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 136, 82–86. doi:10.1016/j.otohns.2006.06.1255

# References

- Karim, A. , Ahmed, S., Siddiqui,R. , Marder, G. S, & Mattana, J. (2002). Severe upper airway obstruction from cricoarytenoiditis as the sole presenting manifestation of a systemic lupus erythematosus flare. *Chest*, 121, 990-993.
- Kinney, W. C. (1999). Rheumatoid pannus of the cervical spine: A case report of an unusual cause of dysphagia. *ENT: Ear, Nose & Throat Journal*, 78(4), 284-291. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10224703>
- Kozora, E., Laudenslager, M., Lemieux, A., & West, S. G. (2001). Inflammatory and hormonal measures predict neuropsychological functioning in systemic lupus erythematosus and rheumatoid arthritis patients. *Journal of the International Neuropsychological Society*, 7(06), 745–754
- Lin, C., Lin, S.-W., Weng, S.-F., & Lin, Y.-S. (2013). Risk of sudden sensorineural hearing loss in patients with systemic lupus erythematosus: a population-based cohort study. *Audiology & Neuro-Otology*, 18, 95–100. doi10.1159/000345512
- Logigian, E., Kaplan, R., & Steere, A. (1990). Chronic neurologic manifestations of Lyme disease. *The New England Journal of Medicine*, 323(21), 1438-1444.<http://doi.org/10.1056/NEJM99011223232102>
- Maciaszczyk, K., Durko, T., Waszczykowska, E., Erkiert-Polguj, A., & Pajor, A. (2011). Auditory function in patients with systemic lupus erythematosus. *Auris, Nasus, Larynx*, 38(1), 26–32. <https://doi.org/10.1016/j.anl.2010.04.008>
- Maneeton,B., Maneeton, N., & Louthrenoo, W. (2010). Cognitive deficit in patientswith systemic lupus erythematosus. *AsianPacific Journal of Allergy and Immunology*, 28(1), 77–83.

# References

- Mayo Clinic. (2015). Juvenile Rheumatoid arthritis: Definition. Retrieved from: <http://www.mayoclinic.org/diseases-conditions/juvenile-rheumatoid-arthritis/basics/definition/con-20014378>
- Mayo Clinic. (2015). Rheumatoid arthritis: Symptoms. Retrieved from: <http://www.mayoclinic.org/diseases-conditions/rheumatoid-arthritis/basics/symptoms/con-20014868>
- Melo, L. F.D., & Da-Silva, S. L. (2012). Neuropsychological assessment of cognitive disorders in patients with fibromyalgia, rheumatoid arthritis, and systemic lupus erythematosus. *Revista Brasileira de Reumatologia*, 52(2), 181-188.
- Mokbel, A. N., Hassan, S. Z., Zohdi, M. I., & ElShennawy, A. M. (2014). Auditory disorders in patients with systemic lupus erythematosus: Relation to clinical parameters. *The Egyptian Rheumatologist*, 36(3), 117-124. <https://doi.org/http://dx.doi.org/10.1016/j.ejr.2014.01.007>
- Muscal, E., & Brey, R. L. (2010). Neurologic Manifestations of Systemic Lupus Erythematosus in Children and Adults. *Neurologic Clinics*, 28(1), 61-73. doi:10.1016/j.ncl.2009.09.004
- Murdin, L., Patel, S., Walmsley, J., & Yeoh, L. H. (2008). Hearing difficulties are common in patients with rheumatoid arthritis. *Clinical Rheumatology*, 27(5), 637-640. <https://doi.org/10.1007/s10067-007-0802-z>

# References

Mursalin, M., & Ahmed, M. S. (2013). Autoimmune swallowing disorders. *Ear, Nose, and Throat Journal*, 92, 538–542.

Öztürk, A., Yalçın, Ş., Kaygusuz, I., Şahin, S., Gök, Ü., Karlidağ, T., & Ardiçoğlu, Ö. (2004). High-frequency hearing loss and middle ear involvement in rheumatoid arthritis. *American Journal of Otolaryngology - Head and Neck Medicine and Surgery*, 25(6), 411–417. <https://doi.org/10.1016/j.amjoto.2004.06.001>

Park, D. C., Glass, J. M., Minear, M., & Crofford, L. J. (2001). Cognitive function in fibromyalgia patients. *Arthritis and Rheumatology*, 44(9), 2125–2133.

Pascual-Ramos, V., Contreras-Yáñez, I., Rivera-Hoyos, P., Enríquez, L., & Ramírez-Anguiano, J. (2014). Cumulative disease activity predicts incidental hearing impairment in patients with rheumatoid arthritis (RA). *Clinical Rheumatology*, 33(3), 315–321. <https://doi.org/10.1007/s10067-014-2485-6>

Prabu, V., Rajasekhar, L., Shanmukhi, Suvarna, a, Agrawal, S., & Narsimulu, G. (2010). O7 Severity of cognitive impairment in SLE is related to disease activity: single center case control study. *Indian Journal of Rheumatology*, 5(3), S4. doi:10.1016/S0973-3698(10)60582-1

Peters, J. E., Burke, C. J., & Morris, V. H. (2011). Three cases of rheumatoid arthritis with laryngeal stridor. *Clinical Rheumatology*, 30, 723–727. doi:10.1007/s10067-010-1657-2

# References

- Raftery, G., He, J., Pearce, R., Birchall, D., Newton, J. L., Blamire, A. M., & Isaacs, J. D. (2012). Disease activity and cognition in rheumatoid arthritis: an open label pilot study. *Arthritis Research & Therapy*, 14(6), R263. doi:10.1186/ar4108
- Rahne, T., Clauß, F., Plontke, S. K., & Keyßer, G. (2017). Prevalence of hearing impairment in patients with rheumatoid arthritis, granulomatosis with polyangiitis (GPA, Wegener's granulomatosis), or systemic lupus erythematosus. *Clinical Rheumatology*, 36(7), 1501–1510. <https://doi.org/10.1007/s10067-017-3651-4>
- Ramos-Remus, C., Duran-Barragan, S., & Castillo-Ortiz, J. D. (2012). Beyond the joints: Neurological involvement in rheumatoid arthritis. *Clinical Rheumatology*, 31, 1–12. doi:10.1007/s10067-011-1841-z
- Roberts, C. M. (2007). Middle ear function in Rheumatoid Arthritis. Master's Thesis
- Roverano, S., Cassano, G., Paira, S., Chiavarini, J., Graf, C., Rico, L., & Heredia, C. (2006). Asymptomatic sensorineural hearing loss in patients with systemic lupus erythematosus. *Journal of Clinical Rheumatology : Practical Reports on Rheumatic & Musculoskeletal Diseases*, 12(5), 217–220. <https://doi.org/10.1097/01.rhu.0000242777.71604.69>
- Salvinelli, F., Cancilleri, F., Casale, M., Luccarelli, V., Di Peco, V., D'Ascanio, L., De Martino, A., &
- Denaro, V. (2004). Hearing thresholds in patients affected by rheumatoid arthritis. *Clinical Otolaryngology and Allied Sciences*, 29, 75–79.
- Sandhya, P., Danda, D., Mathew, J., Kurian, S., & Ramakrishna, B. S. (2012). Eosinophilic esophagitis and pharyngitis presenting as mass lesion in a patient with inactive rheumatoid arthritis. *Journal of Clinical Rheumatology: Practical Reports on Rheumatic & Musculoskeletal Diseases*, 18(1), 33-35. doi: 10.1097/RHU.0b013e31823e6b54

# References

- Shadick, N. A., Phillips, C. B., Sangha, O., Logigian, E. L., Kaplan, R. F., Wright, E. A., . . . Liang, M. H. (1999). Musculoskeletal and neurologic outcomes in patients with previously treated Lyme disease. *Annals of Internal Medicine*, 131(12), 919-26. <http://doi.org/10.7326/0003-4819-131-12-199912210-00003>
- Shadick, N., Phillips, C., Logigian, E., Steere, A., Kaplan, R., Berardi, V., . . . Liang, M. (1994). The long-term clinical outcomes of Lyme disease: A population-based retrospective cohort study. *Annals of Internal Medicine*, 121(8), 560-7. <http://doi.org/10.7326/0003-4819-121-8-199410150-00002>
- Shin, S. Y., Katz, P., & Julian, L. (2013). Relationship between perceived cognitive dysfunction and objective neuropsychological performance in persons with rheumatoid arthritis. *Arthritis Care & Research*, 65(3), 481–6. doi:10.1002/acr.21814
- Sorensen, W. T., Moller-Andersen, K., & Behrendt, N. (1998). Rheumatoid nodules of the larynx. *The Journal of laryngology and otology*, 112(6), 573-574
- Sperling, N. M., Tehrani, K., Liebling, a, & Ginzler, E. (1998). Aural symptoms and hearing loss in patients with lupus. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 118, 762–765. doi:10.1016/S0194-5998(98)70265-7
- Takatsu, M., Higaki, M., & Kinoshita, H. (2005). Ear Involvement in Patients with Rheumatoid Arthritis. *Otology & Neurology*, 26, 755–761.
- Uhlig, T., Moe, R. H., & Kvien, T. K. (2014). The Burden of Disease in Rheumatoid Arthritis. *PharmacoEconomics*, 32(9), 841–851. doi:10.1007/s40273-014-0174-6
- Wilson, B., Greenfield, E., Clare, L., Baddeley, A., Cockburn, J., Watson, P., . . . Crawford, J. (2008). *Rivermead Behavioral Memory Test – Third Edition (RBMT-3)*. New York, New York: Pearson Assessment.