Amyloid-beta plaque detection in a mouse model of Alzheimer’s disease

Anushri Patel

Mentor: Dr. James Olcese
Alzheimer’s Disease

• Alzheimer's disease (AD) is a form of dementia that diminishes cognitive skills and memory
• Two of the major components to AD are formation of amyloid plaques and neurofibrillary tangles
• The effects and damage of AD become more apparent as a person ages
• There is currently no cure but only treatments for symptoms

http://www.alz.org/braintour/healthy_vs_alzheimers.asp
Staining

[Image of brain scans comparing AD and Control groups]

[Image of stained tissue]
Transgenic model

• Many different mouse models--DNA inserted with human genes from familial form of AD
• Double mutation—APP (amyloid precursor protein) site substitution at 670/671 and presenilin 1 exon 9 deletion
• Giving rise to plaques whose number is correlated with loss of learning and memory
• Newer models incorporate tau mutation which more resembles the human disease
My Project Goal

• To optimize techniques in plaque detection as part of the larger ongoing Alzheimer project involving behavioral assessments and other neuropathological measures and analysis of synaptic function
Study Goals

• To understand how the human genes generating the amyloid beta fragments lead to cognitive deficits in the transgenic mouse

• To determine the mechanisms through which plaque development can be slowed
Melatonin

- Hormone naturally produced by the pineal gland
- Neuroprotective function including reduction of plaque load in experiments with high doses
- Mechanism of melatonin: Receptor-mediated or direct effects?

Long-term melatonin administration (0.5 mg/ml) reduces hippocampal and entorhinal cortex β-amyloid load in APP\textsuperscript{sw} +PS1 transgenic mice

Olcese et al 2009
Staining Techniques for Plaques

• Congo Red
• Thioflavin-S & T
• Diaminobenzidine (DAB) immunohistochemistry
• Fluorescence immunohistochemistry
Challenges

- Age of animal
- Perfusions
- Slice thickness
- Dye concentration
- Antibody concentration
- Incubation conditions
- Microscope software
Congo Red-12 months
Congo Red-4 months
DAB only

DAB with nickel
Fluorescence
Summary

• Preliminary results
• Optimize techniques/protocols
• Will be used when cohorts finish behavioral testing and brain tissues are collected
Acknowledgments

• Summer Research Fellowship
• Dr. Olcese
• Lab members—Gina, Katie, Tony, Michelle
• Dr. David Morgan—Johnny Byrd Alzheimer Research Institute Director
• Levenson lab
• Ouimet lab
IMPLEMENTING A MOBILE, SMARTPHONE AED LOCATOR AT FLORIDA STATE UNIVERSITY

Ryan Berger, MSII
Mentor: Nancy Clark
The Florida State University College of Medicine
OBJECTIVES

- Appreciate the importance of timely defibrillation in a cardiac arrest event.
- Understand the role of mobile technology in empowering patients to take charge of their own healthcare.
- Understand the concept of crowdsourcing and how it relates to healthcare.
THE IDEA

- Automated External Defibrillator
- AED/CPR course
- TED talks on role of technology in healthcare and crowdsourcing
- No online map of AEDs on FSU campus
- Peers/faculty/staff unsure of all AED locations in COM
THE FACTS

- 250,000 people die annually in U.S. Of sudden cardiac death
- Time is major factor
  - For every minute resuscitation delayed, survival decreases by 10%.
- Healthcare resources not evenly distributed
- Survival improves as AEDs become easier to use and more available
- Effectiveness of AED device dependent on availability to patient
EFFECTIVENESS OF AED

- Meta-analysis of 1583 cases
- Out-of-hospital cardiac arrest
- Trained non-healthcare professionals
- CPR + early defibrillation with AEDs > survival over CPR alone

THE SOLUTION

- Find responsible party for AEDs at FSU
- Use/build list by walking campus and obtaining contact information
- Compile AED inventory with photos and GPS coordinates
- Incorporate into existing myFSU Mobile app in navigable form
THE PROCESS

- Contact:
  - FSUPD
  - First Responders
  - IT/Blackboard

- Obtain:
  - AED locations with photos and coordinates

- Design/Upload:
  - Navigable AED locator into myFSU Mobile “Places”
The players

Left to right:
Nancy Clark, Faculty Mentor
Debbie Kelly, Assistant Director of Web Services, FSU
Chief David Perry, FSUPD
Dan Bulecza, First Responders Director, FSU
Jesse O’Shea, MSII
THE PRODUCT
AUGMENTED REALITY
DISCUSSION

- What is crowdsourcing?
  - New term
  - Means tapping the power of crowd
  - Crowdsourcing => healthcare
    - Empower patients with tools they need to take charge of their own healthcare
    - Make them part of healthcare team
The Future
REFERENCES


Impact of Short Term Medical Mission trips on the Health Related Quality of Life in Rural Nicaragua

Laura Irastorza & Dr. Daniel Van Durme

FSU College of Medicine
Summer Research Project
Short Term Medical Mission Trips

• Rise in the number of medical students interested in global health and participating in medical mission trips

• Schools adding more programs that allow travel to low-income countries to provide short term care

• Great avenue for professional and educational development of physicians and students

• But do they make a lasting impact on the communities they are serving – specifically on their health related quality of life?

• Very few articles have been published addressing this issue
Health Related Quality of Life (HRQL)

- a multi-dimensional concept that encompasses aspects related to physical health, mental health, emotional health and social functioning

- Focuses on the impact of an individual’s health on their quality of life

- Can be used to measure the effects of chronic illness, treatments, short- and long-term disabilities, and population health

- Several tools have been made to measure HRQL
Health Utilities Index (HUI)

- Health Utilities Index Mark 2 & 3 (HUI2/3)
- Designed to measure the health status of general populations
- Different versions, this one is shorter
  - 40 questions covering vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain
- Been translated in Spanish and previously used in Nicaragua
- Interview administered making it fast and less prone to subject error
- High responsiveness to detect change over time
  - Critical determine the differences between individuals and to identify changes in the community over time
Why Los Cedros, Nicaragua?

- The Florida State University College of Medicine (FSU COM) has built a partnership with the rural community of Los Cedros in Nicaragua

- Visit the community every 3-4 months (4 times a year) since August 2010

- Los Cedros has a population of about 5,000 and about 500 individuals are seen during each week-long trip by FSU
  - About 2000 individuals a year
  - Many individuals come back each trip for refills (continuity of care)

- Individuals range from children to elderly

- So are the mission trips making an impact on their HRQL?
The Study

• Began data collection on August 2012 trip
  — Collected 105 individual HUI2/3 Questionnaires
  — Used iPad to make it electronic and faster

• Cross-Sectional Study: Baseline assessment and community mean score achieved on initial trip. Will re-evaluate in 4-5 years

• Cohort Study: Will continue to follow same sub-population on each subsequent trip for the next 4-5 years
The Study in Action!
Results

• Collected 105 HUI2/3 Questionnaires
• Able to use data from 80 individuals

• 57.14% could move without any difficulty (squat, jump, run, etc)
• 95.23% had good ADL functioning
• 95.23% stated they were generally happy, but 76.19% said at some point they felt anxious, depressed, irritable, or bothered with 40% of those saying they had to seek professional help (30.47% of all 105)
• 80.95% said they had pain or discomfort
HUI Mean Score

- Los Cedros, Nicaragua
- U.S Hispanic Non-Black
- U.S Unselected
- Canada
How would you rate your health over the past 4 weeks?
Discussion

• Majority of individuals seek or want to seek professional help for emotional problems
  – State they feel happy, but often get depressed

• Majority state they have pain or discomfort

• Overall, individuals ranked their health as “regular” which translates to “okay” or “fair”

• Accuracy of results due to only data from 80 of the 105
Limitations

• Time
  – Unable to interview every patient at the clinic (only able to approach 50% of patients, but 100% response rate achieved)
    • Another researcher would help eliminate limitation

• Generalizability of the results
  – Data only from the patients that volunteered to receive medical care and were able to make it to the clinic
    • Lack of male patients (work during the day)
    • Lack of patients too ill to make it to the clinic
      – Random sample is needed to fully generalize results to the Los Cedros Community
      – However, works well for a targeted population of those who continuously use the mission trips as source of health care
Where do we go from here?

• Got a baseline of the HRQL of the Los Cedros community

• Can use this data to help improve FSU’s medical mission trips
  – Cater more to the population it is serving and make changes

• Data can be used for other purposes:
  – National disasters
    • baseline HRQL is recorded and can be used as a goal for relief efforts to bring population back to pre-disaster state.
  – Community improvement programs
    • See how non-medical improvements effect their HRQL
References

• Kanter SL. Global health is more important in a smaller world. *Academic Medicine.* 2008;83(2):115.
Acknowledgments

• Dr. Daniel Van Durme
• Dr. Myra Hurt and the Department of Graduate Research
• Henry Carretta, SPSS analysis
Questions??
Predictive Value of Quix’s Test in the Identification of Selective Canal Involvement in Benign Paroxysmal Positional Vertigo—pre- and post-intervention

Jonathan P Salud, M2
Principal Investigator: Charles G Maitland, MD
"80%...demonstrated turning behavior **contralateral** to the affected semi-circular canal."
Research Goals

• Prospective observational case-series study
• Evaluate Quix’s test in identifying the side of inner ear dysfunction in patients with diagnosis of BPPV.
• Evaluate Quix’s test in identifying residual inner ear dysfunction among BPPV patients following physical therapy intervention.
  – Guides treatment plan
  – May be of great value in reducing risk of falls.
Benign Paroxysmal Positional Vertigo

- **Definition**
  - "Benign Paroxysmal Positional Vertigo (BPPV) is a peripheral vestibular disorder that causes spells of vertigo that last less than 1 minute when the patient moves their head."\(^1\)
    - Provoked by position change

- **Clinical presentation**
  - Chief concern - "Dizziness"
    - "Spinning" sensation
    - Episodic
    - Duration is brief (seconds to minutes)
  - Moving rapidly in "pitch-plane"
    - Getting out of/into bed

BPPV: Epidemiology²

• Peak incidence between 50 and 70 years of age.

• Incidence ranges from 11-64 per 100,000 per year.

• Twice as common in **females** versus males.

• **Posterior semicircular canal** is most common.
  - Horizontal second-most
  - Anterior is quite rare

---

BPPV: Differential

• Differential
  – BPPV
  – Meniere disease
  – Vestibular migraine

• Risk factors
  – Traumatic brain injury
  – Middle ear infection
  – Migraine
  – Family history
  – DM-1, DM-2
BPPV: Treatment

• Non-surgical: Canal repositioning maneuver (CRM)
  – Epley maneuver
  – Semont maneuver
  – Others
  – Medicines largely ineffective

• Surgical
  – Vestibular neurectomy

BPPV: Canalithiasis

Overstimulation of otoliths

Aggregation of otoliths

“plunger effect”
Study Design

• Participants recruited from patients of Balance Disorders Clinic with chief concern of “dizziness.”

• Upon physician dx of BPPV, written informed consent obtained.
Study Design

Initial Visit
- Standard neurologic H&P
- Specific neurologic exam components
  - Past-pointing Test
  - Romberg Test
  - Sharpened Romberg
  - Quix’s Test
- Dix-Hallpike maneuver
- Dynamic Platform Posturography

Physical Therapy Intervention
- Semicircular canal repositioning maneuvers

Follow-Up Visit
- Repeat protocol as per initial visit

Within 1-2 days of initial visit

7-10 days post-intervention
Methods: Quix’s Test

• Two iterations of Quix’s:
  – Standing
    • “arms out”
    • “arms up”
  – Sitting
    • “arms out”
    • “arms up”

• Order of iterations is RANDOMIZED. Not performed in immediate succession.

• Symmetric, unilateral deviation indicative of positive finding (i.e. suggests vestibular dysfunction)
Quix’s Test – “Arms out”

Hypothesis:
The direction of lateralization is **contralateral** to the side of inner ear dysfunction.

Pt arms fully outstretched, with index fingers aligned with examiner’s index fingers.

Pt closes eyes for **thirty seconds**. Observe for lateralization.
Quix’s Test – Variation

“Arms up”

Observe for symmetric, unilateral deviation
Methods: Dix-Hallpike Maneuver

- “Gold standard” diagnostic tool for BPPV
- Patient seated upright on exam table, with legs on exam table.
- Patient head turned 45 degrees off-center, then brought rapidly to supine position.
- Patient asked to achieve maximum ipsilateral lateral gaze.
- Examiner observes for nystagmus.
- Patient returned to seated position
  - Inquiry of vertigo
  - Observation of nystagmus
Methods: Dix-Hallpike Maneuver

- Must achieve ideal acceleration from upright to head-hanging position.
- Once in head-hanging position, **2-5 second latency** prior to onset of nystagmus.
- If nystagmus present, side with ear pointed downward is side of dysfunction
Methods: Dynamic Platform Posturography (DPP)  
Sensory Organization Test (SOT)  

- Evaluates the three components of balance system  
  - Vestibular  
  - Somatosensory  
  - Visual
Methods: Canal Repositioning Maneuver

1. Have patient sit upright, face you (as you stand to patient’s right), and grasp patient’s head with both hands for stability. Help patient to supine position, allowing head to extend just beyond end of examining table, with right ear downward. Maintain position until nystagmus ceases.

2. Move to head of table and reposition hands on sides of patient’s head.

3. Slightly roll patient to left side, rotate head leftward until nose is angled toward floor. Hold position for 30 seconds.

4. As patient rolls onto left side, rotate head leftward until nose is angled toward floor. Hold position for 30 seconds.

5. Help patient into sitting position, facing left.

Source: Laiwani AK; CURRENT Diagnosis & Treatment in Otorhinology – Head & Neck Surgery, 3rd Edition; www.accesssurgery.com

Copyright © The McGraw-Hill Companies, Inc. All rights reserved.
# Results

(As of August 9, 2012)

## TABLE 1

<table>
<thead>
<tr>
<th>Baseline sample characteristics</th>
<th>n = 56&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>n = 47</td>
</tr>
<tr>
<td>Mean, SD</td>
<td>65.085, 11.417</td>
</tr>
<tr>
<td>Range</td>
<td>[30, 85]</td>
</tr>
<tr>
<td>Sex [n (%)]</td>
<td>n = 51</td>
</tr>
<tr>
<td>Male</td>
<td>[13 (25.49)]</td>
</tr>
<tr>
<td>Female</td>
<td>[38 (74.51)]</td>
</tr>
<tr>
<td>Race [n (%)]</td>
<td>n = 34</td>
</tr>
<tr>
<td>White</td>
<td>[23 (67.65)]</td>
</tr>
<tr>
<td>African-American</td>
<td>[11 (32.35)]</td>
</tr>
<tr>
<td>Symptom duration (days)</td>
<td>n = 31</td>
</tr>
<tr>
<td>Mean, SD</td>
<td>347.355, 714.025</td>
</tr>
<tr>
<td>Range</td>
<td>[7, 3650]</td>
</tr>
</tbody>
</table>

<sup>a</sup>Total participant enrollment as of 8/9/2012.
# Results: Future Aims

**TABLE 2**

*Quix’s test vs. SOT (Vestibular)*

<table>
<thead>
<tr>
<th>PRE – INTERVENTION</th>
<th>“FAIL” SOT (Vestibular)</th>
<th>“PASS” SOT (Vestibular)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+) Quix’s test</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>(-) Quix’s test</td>
<td>c</td>
<td>d</td>
</tr>
</tbody>
</table>

Sensitivity, specificity, PPV, NPV, OR

**TABLE 3**

*Dix-Hallpike vs. SOT (Vestibular)*

<table>
<thead>
<tr>
<th>PRE – INTERVENTION</th>
<th>“FAIL” SOT (Vestibular)</th>
<th>“PASS” SOT (Vestibular)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+) DH</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>(-) DH</td>
<td>c</td>
<td>d</td>
</tr>
</tbody>
</table>

Sensitivity, specificity, PPV, NPV, OR
Conclusions

• The study is ongoing per protocol, which aims for \( n = 100 \).

• To date, the data supports our initial hypothesis regarding the relationship between side of Quix lateralization and side of inner ear dysfunction (i.e. contralateral)
Future Directions

• Observing length of time following CRM and/or number of CRM sessions needed until symptoms resolve may better characterize the time course of patient care plan.

• ENG performed on all study participants. Provides quantified measure of nystagmus.

• Investigate residual canalithiasis and incidence of falls among at-risk patients
  — Geriatric patients w/ BPPV
Peer Acknowledgements

Shawn Adams (M2)       Ryan Brosch (M2)
Acknowledgements

John P Fogarty, MD
Myra M Hurt, MD
Charles G Maitland, MD
Timothy Booker, PA
Theresa Hunter, PhD
Balance Disorders Clinic
Tallahassee Memorial Hospital
FSU COM Division of Research, Graduate and Undergraduate Programs
Thank you for your attention.

Questions?

(go noles!)
Service Work and Nutritional Education in Santa Marta, Colombia

By Maureen Bruns
References

“Our mission is to help the children and families we work with access the tools they need to fight poverty and social injustice. By empowering them through education, information and health support, we give them the chance to spread their wings and reach their full potential as proud, enthusiastic and effective members of their communities.”
Fundadores
Oasis
Oasis – Sports Day
Nutrition Workshops
Puppet Shows