Supporting Aging Adults with Down Syndrome and Alzheimer’s Disease

Global Down Syndrome Foundation’s Webinar Series

Presenters: Martha Keele, Dr. Huntington Potter, Bryn Gelaro

Tuesday, October 30th, 2018
The Global Down Syndrome Foundation is part of a network of affiliate organizations that work closely together on a daily basis to deliver on our mission, vision, values, and goals:

**Global & Affiliates**

- **Global**: was established as a 501(c)3 in 2009 and is “Dedicated to significantly improving the lives of people with Down syndrome through Research, Medical Care, Education, and Advocacy”

- **Affiliates are**:
  - Established with a lead gift from Anna & John J. Sie Foundation
  - Must work closely together to benefit people with Down syndrome
  - Must be self-sustaining financially
Aging and Alzheimer’s Disease
In
People with Down Syndrome

Huntington Potter, Ph.D.
Rocky Mountain Alzheimer’s Disease Center
Department of Neurology
Linda Crnic Institute for Down Syndrome
CU Denver/AMC
First Report of Down Syndrome

John Langdon Down, 1866
First Report of Alzheimer’s Disease

“I have lost myself.”

Alois Alzheimer, 1907

RESEARCH TODAY, MEMORIES FOREVER
THE PROBLEM: Alzheimer’s Disease

- 5.7 million patients
- $277 billion annual cost
- $1.1 trillion by 2050
- 10% of people over age 65
- 40-50% of people over age 85

Down Syndrome

- ~400,000 patients
- ~$19 billion annual cost
- 1/700 live births
- 100% acquire features of AD

RESEARCH TODAY, MEMORIES FOREVER
Care: Memory Disorders Clinic

- Academic medical center (new clinic location!)
  - 6 Behavioral Neurologists
  - 1 Neuropsychologist
  - 2 Advanced Practice Providers
  - 1 Fellow
  - 3,500 patient visits/year
- World-class memory care
  - Accurate diagnosis
  - Latest treatments
- Opportunities to participate in research
  - Clinical Trials
  - Longitudinal Studies
Current Alzheimer’s Drugs Only Enhance the Way Neurons Communicate with Each Other

Synapse

- Namenda (memantine)
- Aricept (donepezil)
- Razadyne (galantamine)
- Exelon (rivastigmine)
Long-Term Solution: MORE RESEARCH

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First Molecular Advance in Alzheimer’s Disease and Down Syndrome

Normal Brain

Alzheimer

Plaques and tangles

George Glenner and Caine Wong 1984

DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA

Aβ Peptide
The Amyloid Precursor Protein Gene Is Encoded on Chromosome 21

The ‘Swedish’ Alzheimer’s disease family inherits a mutant APP gene
PiB–PET: Amyloid Imaging in Alzheimer’s

A
Normal

B
Amyloid-Positive

Proenzano, JAMA Neurol, 201
Correlating Pathology with Dementia

# of Neurons

Plaques & Brain blood vessel damage

Tangles

Non-demented (Preclinical AD) | Non-demented | Very mild AD (MCI) | Mild AD | Mod AD | Sev AD

Adapted from Craig-Schapiro, Fagan, and Holtzman, Neurobiol Dis. 2009 August;35(2):128-140.
Mice with mutant human APP gene accumulate amyloid deposits
Measuring Short-Term Memory in Mice

The Radial Arm Water Maze
The Amyloid Cascade in Alzheimer’s

Amyloid Precursor Protein (APP)

sAPPβ → β-secretase → γ-secretase → Aβ → Aβ deposition in amyloid plaques
Eli Lilly: Solanezumab (LY2062430)  
(Anti-amyloid antibody)  
Phase III study terminated due to unlikely efficacy

Lundbeck: Idalopirdine (Lu AE58054)  
(5HT6 antagonist designed to increase release of acetylcholine)  
Three failed Phase III trials due to lack of efficacy

**BACE Inhibitors:**  
Eli Lilly, AstraZeneca, Merck
Potential Successes in Alzheimer’s Trials

**Anti-Amyloid Antibodies**

**Biogen: Aducanumab (BIIB037)**
- (Recruiting/treating in Phase III trial)
- Currently recruiting for multi-year Phase III trial, including at CU Anschutz

**Biogen and Esai: BAN2401 (mAb158)**

**Lilly: LY3002813 (N3pG-Aβ)**

**Roche: Gantenerumab (RO4909832)**

**BACE Inhibitors**

**Lilly: LY3202626 plus N3pG-Aβ**

**Esai and Biogen: Elenbecestat (E2609)**
Sleep Disorders Predate Alzheimer’s

- Out of 516 cognitively normal adults (71-78 years old), those with sleep disordered breathing showed greater accumulation of beta-amyloid deposits over a three-year period

Wheaton College
Previous Stress Is Related to Poorer Cognition/Memory, Especially in African Americans

- Each stressful event aged the brain 1.5 years in non-Hispanic whites and 4 years in African Americans

University of Wisconsin
Mediterranean or MIND Diets May Reduce Alzheimer’s Risk

- Reduced risk of dementia by 1/3
- Diet rich in plants, olive oil, fish, etc.

POINTER trial, which includes aerobic workouts plus the MIND diet

UCSF
Why are People with Rheumatoid Arthritis Protected Against Alzheimer’s Disease?
GM-CSF Reduces Aβ Deposition in AD Mouse Brain

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GM-CSF Improves Cognition in Aged DS and Normal Mice

Dp16 mice + GM-CSF Control + GM-CSF

Time to reach platform (s)

Baseline, Post-treatment

P = 0.02

P = 0.001
Improved MMSE in GM-CSF-Treated Subjects Compared to Placebo-Treated Subjects

\[ P = 0.0008 \text{ (from baseline)} \]

\[ P = 0.0135 \text{ (vs. placebo)} \]
GM-CSF Treatment May Reduce Amyloid Load

$\text{SUVr normalized to radiation dose:}$

$\text{SUVr-N = SUVr} \times (10\text{mCi/radiation dose in mCi})$

Placebo: +3.74%

GM-CSF: -14.23%

$P = 0.0229$
GM-CSF Trial Summary

Current 3-Week Trial:
- 5 GM-CSF injections/week for 3 weeks
- Total 40 subjects; Amyvid® PET for last 20 subjects

Results as of Today:
- 34 subjects finished treatment phase
- No evidence of vasogenic edema or hemorrhage or any other serious adverse events
- Potential improvement in MMSE/cognition at end of treatment
- Possible reduced amyloid load

Future 6-Month Trial:
- 5 GM-CSF injections/week for 6 months; 42 subjects
  $1,000,000 Part The Cloud grant from the Alzheimer’s Association

Websites:
- trialmatch.alz.org
- ClinicalTrials.gov
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Colorado University Results CURE

Anschutz Medical Campus

Dementia on the rise
Alzheimer’s Patients in the U.S.

Hope!
Behavior recommendations to support aging adults with Down syndrome and Alzheimer’s Disease

By: Bryn Gelaro, LSW
Director of Adult Initiatives and Special Projects
Global Down Syndrome Foundation
Some adults will develop symptoms and signs of Alzheimer’s disease
- Some will not

Not a simple way to diagnose

Most families do not have access to medical experts on Down syndrome
- Misdiagnosed
- Unable to receive correct diagnosis

Still need to know how to support their adults!
On the topic of aging and older adults Down syndrome

- **Change, loss and decline**
  - Tend to be the focus of providers seeing aging adults with or without Alzheimer’s disease

- **Understanding change in functioning for the sake of supporting a healthy aging process**
  - What can they still do?
  - What do they still enjoy?

- **Responsive and highly attuned caretaking is key!**

- **Delicate balance**
3 Key Behavior Recommendations for supporting adults with Down syndrome and Alzheimer’s Disease

1. Maintaining sense of community and engagement

2. Reducing negative effects of behavior changes

3. Supporting caretaker
As aging or dementia processes occur, people’s worlds tend to get smaller
- Both caretaker and self-advocate

Can be helpful towards end of life, but can also negatively impact overall health and mental state
- Depression, Anxiety
- ‘Use it or lose it’ idea
- Protective factors: diet, exercise, social engagement

As long as they can tolerate it, change scope of activity or social event instead of quitting it all together
Socialization and connection is so important

Modify schedule/plans to meet current level of need

Only push to the degree they can tolerate

If something is a battle, consider if impact is worth it or if desired outcome can be achieved another way

Example: Want to keep them going to music class but mornings tend to move so slowly and rushing them makes it worse
Activities that are still stimulating but are less physically demanding: car rides, puzzles, cards, painting and photobooks

Volunteering—especially involving animals!

Join them in activity or fantasy play!
   - Example: If stuck in self talk, roleplay with them
   - Example: Activities that involve minimal verbal/quick on your feet exchange

May have an easier time with recalling things from a long time ago than learning new things
   - Encourage them to keep doing things they’ve always enjoyed
Changes we see typically involve:
- Mood, interests, speech, mobility (slowing/fearfulness), visual/hearing, completing ADLs, dropped routines

Consistency is so important now more than ever

Making their world smaller if become fearful or confused
- Goal provide safety
- Fewer new people and new places
- Reminders, verbal prompts, and visual aids!
  - Example: Photobooks of family/staff/friends
Reducing negative effects of behavior changes

continued…

❖ Talk to your aging adult about what’s going on and what they are feeling!
  ❖ These changes are scary for them, too!
  ❖ Involve them in conversations
  ❖ Empathy and safety, even when you don’t have answers

❖ Maximize autonomy and skill
  ❖ Focus on what they can do, not the things that are becoming challenging
  ❖ An aging adult is loosing skills and may feel out of control
  ❖ Find ways to increase/maintain involvement

❖ Do not assume everything is just Alzheimer’s Disease!
Reducing negative effects of behavior changes

Keep track of changes you notice:

- Create a baseline for reference
- Change and decline is uneven and sometimes plateau
- These will help you and your adult’s providers understand changes and anticipate potential supports
Reducing negative effects of behavior changes

continued...

- Repetition & forgetting
  - Where am I, am I going to work now, where is ___?

- Safety
  - Stairs
  - Eating/Choking
  - Depth Perception (toileting, transferring in cars)
  - Eloping/walking out
  - Bathing
Perception and visual depth tends to weaken with age and in adults with Alzheimer’s disease Dementia
- Can increase fearfulness, confusion, mistrust of environment, withdraw socially

Inability to judge and perceive the situation can impact ability to feel comfortable and safe

Tips- Especially important for spaces where physical transitions occur!
- Contrasting colors
- Dark surfaces look like a hole
- Avoid highly patterned flooring
Families report: “Stubbornness” or “unresponsiveness” increases
- Saying “no” to activities
- Slowing down pace
- Not listening

- Awareness of confusion, notice they can’t do as much for themselves
- They are grasping for things they can control
Caring for a person can be exhausting, frustrating, saddening, depressing

- Don’t underestimate the tole this takes on yourself as a caretaker or family member
- Does not make you a bad parent or caretaker
- With AD you are experiencing a loss and you may begin to grieve while your family member is still alive

Respite care supports

Use your resources and build in breaks

- You will be more patient, tolerant, and healthy in the long run
Be aware of “Parallel Decline”

Life planning prior to aging, involving adult with Down syndrome

Support Groups

Attendees or organizers: Be aware of the many stages of aging/illness/grief!
References and Resources

- *Mental Wellness in Adults with Down Syndrome* by Dr. Brian Chicoine and Dr. Dennis McGuire

- *Let’s Talk about Dementia- Workbook* by Down’s Syndrome Scotland (Downloadable)

- Chicago Adult Down Syndrome Center
  - Online Resources for Families & Caregivers
Thank You!

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&
Dr. Huntington Potter