

The Specific Aims Page: A Primer

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Why the Aims Matter

- Specific Aims are your first, main, most important opportunity to grab the reader's attention and interest them in your project
- It may be the only page some reviewers read!
- Once you have a good Aims, it is a highly useful document to send to colleagues, mentors, co-investigators to introduce your work and solicit feedback
- Solid aims structure and facilitate writing the rest of the application-- each sentence will be a paragraph/subheading of your research strategy, and what you hypothesize dictates the assessments and power analysis

SF424 Instructions—Forms F

- State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the proposed research will have on the research field(s) involved.
- List succinctly the specific objectives of the research proposed (e.g., to test a stated hypothesis, create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology).

General Principles

- Start early (at least 2 months out from deadline) and plan to go through MANY revisions
- Every word in the aims is precious—labor over each one and mete them out judiciously
 - Reverend Maclean’s commandment: “Again, half as long.”
- Consider each sentence a distinct idea taking the reader a single step in the argument
- Initiate a style that you will carry through the application uniformly
- Make things easy on reviewers—they are “cranky”

Structure of Aims

- P1: Introduction/Background
- P2: Overview of Project
- P3: Aims and Hypotheses
- P4: Significance and Innovation

2. SPECIFIC AIMS

BACKGROUND: Hearing loss (HL) is associated with Major Depressive Disorder (MDD) in older adults, but the neural and behavioral mediators linking these prevalent and disabling conditions are unknown. Moderate HL triples risk for incident MDD, and we have shown that even hearing loss at a level still considered "normal" is associated with depression risk. Reduced transmission of auditory stimuli results in deafferentation-induced fronto-temporal atrophy, recruitment of the cognitive control network (CCN) to support effortful listening, and impairments in emotion processing, all of which are neural circuits highly relevant to MDD. Tinnitus, a common co-traveler with age-related HL, independently is associated with neurocognitive dysfunction, depression and suicidal ideation, and aberrant amygdala reactivity. Older adults with HL often avoid or withdraw from social contexts in which background noise will make it difficult to communicate, resulting in social isolation and loneliness, which themselves cause cognitive and physical decline, psychiatric disorders, and increased mortality. Pilot work by our group suggests that hearing aids have beneficial effects on depressive symptoms and executive function, but larger studies are needed. It is unknown whether hearing aids affect mood through improved cognitive control, normalization of emotion processing, resolution of tinnitus, increased social engagement, or a combination of these factors. Knowledge of therapeutic mechanisms would enhance our understanding of pathophysiologic relationships and provide actionable information about treatment targets given hearing aids alone may be insufficient to result in MDD remission.

OVERVIEW: The goals of this proposal are to better understand the pathophysiology linking HL and MDD in older adults, determine whether hearing rehabilitative treatment is effective for MDD, and identify mechanisms by which improved hearing capacities result in decreased depression. Toward that end we propose randomizing 150 older adults with HL/MDD to receive hearing aids (HA, N=75) or a control condition (healthy aging education, N=75) for 12 weeks. Audiometric testing, psychiatric evaluation, cognitive assessment, and characterization of social engagement will be performed at baseline, 6 weeks, and at 12-week study endpoint. Multimodal magnetic resonance imaging (MRI) focused on neural circuits underlying auditory perception, cognitive control, and emotion processing will be conducted at baseline and 6 weeks. Based on our pilot data and the broader literature, we believe hearing aids will lessen the cognitive burden imposed by effortful listening and facilitate the processing of emotionally-valenced auditory stimuli, thereby improving executive functioning and emotion regulation. Restoration of hearing may also lessen tinnitus and result in improved social engagement, which will contribute to reduced depressive symptoms. The present investigative team is ideally situated to conduct the proposed work: we have established the risk posed by HL for MDD, undertaken rigorously designed randomized controlled trials of hearing aids for MDD, and built theoretical models of the mediators linking HL and MDD in older adults.

AIM 1: To elucidate baseline relationships between hearing capacities, indices of brain health, and cognitive/affective functioning.

Hyp 1: Poorer hearing (higher thresholds on pure tone audiometry, poorer speech discrimination) will be associated with auditory system atrophy and lower integrity of cognitive control and emotion processing networks (functional connectivity [rs-fMRI] and BOLD activity [Simon and Emotion Task fMRI]) at baseline.

AIM 2: To investigate whether hearing aids are effective for MDD in older adults with HL.

Hyp 2: Compared to the education control, hearing aids will result in greater improvements in depressive symptoms (Hamilton Rating Scale for Depression [HRSD]) and executive functioning (NIH Toolbox) at 12 weeks.

AIM 3: To identify neural and behavioral features mediating the effect of hearing aids on depression.

Hyp 3: Week 6 improvement in CCN connectivity/activations, emotion processing network connectivity/activations, tinnitus severity, and social engagement each will partially mediate the beneficial effect of hearing aids on depression severity at 12 weeks.

Exploratory aim: To identify patient-level moderators (i.e., hearing variables, cognitive profile, social network/support) of the effect of hearing aid treatment on depressive symptoms.

SIGNIFICANCE AND INNOVATION: This will be the first study to comprehensively interrogate brain structure, cognitive and affective functioning, and depressive symptoms in older adults with hearing impairment, thereby providing unique mechanistic information about these interconnected entities. Effective treatments for hearing impairment exist, but their utilization by older adults is strikingly low. Demonstrating that hearing aids improve depressive symptoms, executive function, and brain health in older adults will facilitate education efforts and maximize the public health benefits of the OTC Hearing Aid Act of 2017. Results from this study also will contribute to rationally designed novel therapeutics for LLD that are based upon an understanding of how aging-related processes interact with the pathophysiology underlying psychiatric disorders.

2. SPECIFIC AIMS

BACKGROUND: Hearing loss (HL) is associated with Major Depressive Disorder (MDD) in older adults, but the neural and behavioral mediators linking these prevalent and disabling conditions are unknown. Moderate HL triples risk for incident MDD, and we have shown that even hearing loss at a level still considered "normal" is associated with depression risk. Reduced transmission of auditory stimuli results in deafferentation-induced fronto-temporal atrophy, recruitment of the cognitive control network (CCN) to support effortful listening, and impairments in emotion processing, all of which are neural circuits highly relevant to MDD. Tinnitus, a common co-traveler with age-related HL, independently is associated with neurocognitive dysfunction, depression and suicidal ideation, and aberrant amygdala reactivity. Older adults with HL often avoid or withdraw from social contexts in which background noise will make it difficult to communicate, resulting in social isolation and loneliness, which themselves cause cognitive and physical decline, psychiatric disorders, and increased mortality. Pilot work by our group suggests that hearing aids have beneficial effects on depressive symptoms and executive function, but larger studies are needed. It is unknown whether hearing aids affect mood through improved cognitive control, normalization of emotion processing, resolution of tinnitus, increased social engagement, or a combination of these factors. Knowledge of therapeutic mechanisms would enhance our understanding of pathophysiologic relationships and provide actionable information about treatment targets given hearing aids alone may be insufficient to result in MDD remission.

OVERVIEW: The goals of this proposal are to better understand the pathophysiology linking HL and MDD in older adults, determine whether hearing rehabilitative treatment is effective for MDD, and identify mechanisms by which improved hearing capacities result in decreased depression. Toward that end we propose randomizing 150 older adults with HL/MDD to receive hearing aids (HA, N=75) or a control condition (healthy aging education, N=75) for 12 weeks. Audiometric testing, psychiatric evaluation, cognitive assessment, and characterization of social engagement will be performed at baseline, 6 weeks, and at 12-week study endpoint. Multimodal magnetic resonance imaging (MRI) focused on neural circuits underlying auditory perception, cognitive control, and emotion processing will be conducted at baseline and 6 weeks. Based on our pilot data and the broader literature, we believe hearing aids will lessen the cognitive burden imposed by effortful listening and facilitate the processing of emotionally-valenced auditory stimuli, thereby improving executive functioning and emotion regulation. Restoration of hearing may also lessen tinnitus and result in improved social engagement, which will contribute to reduced depressive symptoms. The present investigative team is ideally situated to conduct the proposed work: we have established the risk posed by HL for MDD, undertaken rigorously designed randomized controlled trials of hearing aids for MDD, and built theoretical models of the mediators linking HL and MDD in older adults.

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SIGNIFICANCE AND INNOVATION: This will be the first study to comprehensively interrogate brain structure, cognitive and affective functioning, and depressive symptoms in older adults with hearing impairment, thereby providing unique mechanistic information about these interconnected entities. Effective treatments for hearing impairment exist, but their utilization by older adults is strikingly low. Demonstrating that hearing aids improve depressive symptoms, executive function, and brain health in older adults will facilitate education efforts and maximize the public health benefits of the OTC Hearing Aid Act of 2017. Results from this study also will contribute to rationally designed novel therapeutics for LLD that are based upon an understanding of how aging-related processes interact with the pathophysiology underlying psychiatric disorders.

Introduction/Background

- Elements of an effective introduction:
 - Great first sentence that grabs the reader's attention—avoid “Bad things happen to many people”
 - Concisely and clearly explain what is known
 - Outline the gap in knowledge that you will be addressing
 - Identify why it is important to fill this gap—the critical need for your research
- Writing style for educated non-specialists (save the confusing details for the research strategy)
- Limit abbreviations or undefined confusing terms
- In discussing how the literature has evolved and its current state, consider privileging work you have done

Example

BACKGROUND: As hearing loss (HL) is a risk factor for Major Depressive Disorder (MDD) in older adults, its treatment with hearing aids appears to improve MDD, but the neural and behavioral mediators linking these prevalent and disabling conditions are unknown. Moderate hearing loss triples risk for incident MDD, and we have shown that even hearing loss at a level still considered “normal” is associated with depression risk. Reduced transmission of auditory stimuli results in deafferentation-induced fronto-temporal atrophy, recruitment of the cognitive control network (CCN) to support effortful listening, and impairments in emotion processing, all of which are neural circuits highly relevant to MDD. Tinnitus, a common co-traveler with age-related HL, independently is associated with neurocognitive dysfunction, depression and suicidal ideation, and aberrant amygdala reactivity. Older adults with HL often avoid or withdraw from social contexts in which background noise will make it difficult to communicate, resulting in social isolation and loneliness, which themselves cause cognitive and physical decline, psychiatric disorders, and increased mortality. Pilot work by our group suggests that hearing aids have beneficial effects on depressive symptoms and executive function, but larger studies are needed. It is unknown whether hearing aids affect mood through improved cognitive control, normalization of emotion processing, resolution of tinnitus, increased social engagement, or a combination of these factors. Knowledge of therapeutic mechanisms would enhance our understanding of pathophysiologic relationships and provide actionable information about treatment targets given hearing aids alone may be insufficient to result in MDD remission.

Example

1st sentence to grab

what is known

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what is unknown

why important

Overview of Project

- The “Who, What, Why” Paragraph
- This is where you say, “Ok, so to address this crucial gap in human knowledge, here is what we are going to do.”
- Major points:
 - Long term goal of the work
 - Your central hypothesis and solution to the knowledge gap
 - Rationale
 - You and your team’s qualifications
- Can be used to briefly summarize the basic elements of the project

Example

OVERVIEW: The goals of this proposal are to better understand the pathophysiology linking HL and MDD in older adults, determine whether hearing rehabilitative treatment is effective for MDD, and identify mechanisms by which improved hearing capacities result in decreased depression. Toward that end we propose randomizing 150 older adults with HL/MDD to receive hearing aids (HA, N=75) or a control condition (healthy aging education, N=75) for 12 weeks. Audiometric testing, psychiatric evaluation, cognitive assessment, and characterization of social engagement will be performed at baseline, 6 weeks, and at 12-week study endpoint. Multimodal magnetic resonance imaging (MRI) focused on neural circuits underlying auditory perception, cognitive control, and emotion processing will be conducted at baseline and 6 weeks. Based on our pilot data and the broader literature, we believe hearing aids will lessen the cognitive burden imposed by effortful listening and facilitate the processing of emotionally-valenced auditory stimuli, thereby improving executive functioning and emotion regulation. Restoration of hearing may also lessen tinnitus and result in improved social engagement, which will contribute to reduced depressive symptoms. The present investigative team is ideally situated to conduct the proposed work: we have established the risk posed by HL for MDD, undertaken rigorously designed randomized controlled trials of hearing aids for MDD, and built theoretical models of the mediators linking HL and MDD in older adults.

Example

long term goals

summary and solution to
knowledge gap

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rationale and central
hypotheses

team's qualifications

Aims and Hypotheses

- Briefly describe each aim and accompanying hypothesis(es). Usually the aim is worded more broadly and the hypothesis more focused.
- Generally 2-4 aims with associated Hyp and possibly sub-Hyp. People vary on Exploratory Aims.
- Be precise and specific; provide names of the primary outcome measures and directions of effects.
- They should be clear, achievable, and familiar to readers from the foregoing Introduction and Overview
- Use active language and avoid rote repetition of phrases
- Aims should be related but not dependent upon each other
- No purely descriptive aims (ie fishing)
- No matter how the hypothesis testing works out, be able to accomplish the aim

Example

- 3 Aims and 1 Expl
- Not dependent
- Reasonably clear and specific
- No descriptive aims

AIM 1: To elucidate baseline relationships between hearing capacities, indices of brain health, and cognitive/affective functioning.

Hyp 1: Poorer hearing (higher thresholds on pure tone audiometry, poorer speech discrimination) will be associated with auditory system atrophy and lower integrity of cognitive control and emotion processing networks (functional connectivity [rs-fMRI] and BOLD activity [Simon and Emotion Task fMRI]) at baseline.

AIM 2: To investigate whether hearing aids are effective for MDD in older adults with ARHL.

Hyp 2: Compared to the education control, hearing aids will result in greater improvements in depressive symptoms (Hamilton Rating Scale for Depression [HRSD]) and executive functioning (NIH Toolbox) at 12 weeks.

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Significance and Innovation

- At their own peril, some neglect this and/or repeat a few sentences from the background
- Keep some of your powder dry from the Introduction—you don't want to be left with a dry repetition in the last paragraph
- Close the loop back to the first sentence by identifying the specific ways your project will be valuable to the funding agency, the field, and society

Example

SIGNIFICANCE AND INNOVATION: This will be the first study to comprehensively interrogate brain structure, cognitive and affective functioning, and depressive symptoms in older adults with hearing impairment, thereby providing unique mechanistic information about these interconnected entities. Effective treatments for hearing impairment exist, but their utilization by older adults is strikingly low. Demonstrating that hearing aids improve depressive symptoms, executive function, and brain health in older adults will facilitate education efforts and maximize the public health benefits of the OTC Hearing Aid Act of 2017. Results from this study also will contribute to rationally designed novel therapeutics for LLD that are based upon an understanding of how aging-related processes interact with the pathophysiology underlying psychiatric disorders.

Example

innovation

significance

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loops back to background

Writing Tips

- Be open to revision, even rather late in the game (but not too late)
- Be a good receiver of feedback, and don't be unnecessarily attached to your initial ways of presenting things
- You may consider a figure or graphic on the Aims page, but use caution since you have so little space available
- Go easy on underlining, bold, etc. A little goes a long way.
- Usually do not need references as they distract and will be found in Strategy
- Acquire and read as many specific aims pages as possible—observe and appreciate all the different ways to get across the same information
 - None of my funded aims provided the perfect example for this class!

Resources

- NIH REPORTER—review project summaries there, which are often cut and pasted from investigator's aims pages
- Monte and Libby. Introduction to the Specific Aims Page of A Grant Proposal, Acad Emerg Med 2018; 25:1042-1047.
- Russell and Morrison, The Grant Application Writer's Workbook
- Feel free to contact me with any questions! brr8@cumc.columbia.edu