

ix. Development of New Cognitive and Functional Instruments (DNCFI)

Competition Objectives: The Alzheimer's Association is launching a new initiative to stimulate the scholarly investigation and development of cognitive or functional evaluation instruments that can capture the earliest changes in the disease, are sensitive to change over time, and/or could be used in clinical trials. This RFA is designed to enable pilot research or proof-of-principle studies that can provide preliminary data for subsequent inquiry.

Background: It is now well recognized that the key underlying brain changes that lead to Alzheimer's disease are present many years before the clinical diagnosis. Further, the cognitive and functional changes develop gradually over time, well before a clinical diagnosis of dementia is warranted. The intense focus on the earliest preclinical stages of AD calls for a concomitant focus on developing cognitive or functional instruments that are suitable for measuring these changes.

Intervention studies have also begun to focus on mildly impaired individuals who may or may not develop dementia, and new trials are contemplated that will focus on individuals without any detectable cognitive changes who are shown by amyloid PET or other biomarkers to be at risk for progressing to Alzheimer's disease. These studies will require a new generation of instruments that can characterize the earliest cognitive and functional changes and that can reliably assess change in performance over time. Traditional global cognitive tests, typically used in intervention trials, are not optimal for reliably detecting subtle cognitive changes over time, particularly in older adults with very mild cognitive problems.

Potential themes: The Association seeks proposals to develop new methodologies for assessing subtle cognitive and functional performance, particularly among those not yet diagnosed with dementia. Ideally such instruments could reliably capture cognitive or functional change or decline in its early stages and be available in formats that would be amenable for use in clinical trials. Optimally such measures would eventually be demonstrated to be sensitive to underlying AD-related brain changes, thus providing clear validity to the measurements. These new instruments could be more improved versions of extant neuropsychological and functional evaluations or newly designed cognitive instruments. They could be paper and pencil or computerized, self- or informant-administered. We recognize that large-scale prospective validation studies may be beyond the scope of this RFA, but anticipate that instruments developed via this RFA should be compelling candidates for such validation studies in the future.

Grant proposals may address, but are not limited to, the following areas of study:

1. Use modern psychometric techniques, such as item response theory, to improve and modify existing instruments, or develop new testing schemes such as assessment bursts to capture an individual's change in performance over time.
2. Use existing knowledge of AD-related brain changes to develop theory-based cognitive or functional assessments that might be sensitive to very early changes.

3. Conduct cross-sectional studies or prospective studies relevant to participant groups to establish the potential of instruments to capture early changes.
4. Investigate psychometric properties of new instruments (such as concurrent/discriminant validity, test-retest reliability, etc.).
5. Relate instrument performance to other markers of disease-related change such as biomarkers or imaging measures.
6. Establish testing/monitoring platforms for measuring performance over time.
7. Develop improved observation-based measures of cognition or function that are sensitive to the earliest functional changes.

General considerations: Any proposal must have a clear focus on ADRD and on cognitive or functional assessment. All proposals should clearly and explicitly outline the measure to be investigated, the methods for study, sample, outcomes, etc. The ultimate goal is to develop new measures or significantly improve established measures that could then be used in clinical practice and therapeutic trials.

The Alzheimer's Association recognizes the need to increase the number of scientists from underrepresented groups in the research enterprise. Researchers from these groups are encouraged to apply.

Funding and award period: The Association anticipates funding up to 2 approaches addressing needs in cognitive and functional instrument development. Each award is limited to \$400,000 (direct and indirect costs) for two to three years. Requests in any given year may not exceed \$200,000 (direct and indirect costs). Indirect costs are capped at 10 percent (rent for laboratory/office space is expected to be covered by indirect costs paid to the institution).

Eligibility: Researchers with full-time staff or faculty appointments are encouraged to apply. Applications from post-doctoral candidates will not be accepted.

Deadlines and award dates: Letters of Intent must be received by 5:00 PM EASTERN STANDARD TIME, December 20, 2011. Letters of Intent will not be accepted after this date. No exceptions will be made.

Applications must be received by 5:00 PM EASTERN STANDARD TIME, February 7, 2012. Scientific and technical review will be conducted from March through June 2012.

The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2012. Funding will be awarded by late July/early August 2012.

Mechanism of award, reporting requirements and allowable costs: The mechanism of the award is the individual research grant. The maximum allowable duration is three years. Annual scientific progress and financial reports are required. Continuation of the grant over the awarded duration is contingent upon the timely receipt of scientific progress and financial reports.

Budget: A “budget summary” for the proposed research project is required and must be submitted with the application and within the allowable page limits. However, if the application is to be awarded, a more detailed budget will be required and must be approved before the disbursement of funds. Your budget must not exceed the maximum amount of the award (\$400,000 for the development of new cognitive and functional instrumentation).

Allowable costs under this award: It is required that most of the funds awarded under this program be used for direct research support.

Allowable costs under this award include:

- Purchase and care of laboratory animals
- Small pieces of laboratory equipment and laboratory supplies
- Computer equipment if used strictly for data collection
- Travel (up to \$1,000 per year)
- Salary for the principal investigator, scientific (including post-doctoral fellows) and technical staff (including laboratory technicians and administrative support staff whose work is directly related to the funded project)

Costs not allowed under this award include:

- Tuition
- Computer hardware or software for investigators
- Rent for laboratory/office spaces
- Construction or renovation costs

For more information: Contact grantsapp@alz.org or call 1.312.335.5747 or 1.312.335.5862.