Validity of the Electronic Self-Administered Gerocognitive Examination (eSAGE) – Smartphone

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Protocol

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Introduction

Cognitive impairment is becoming increasingly prevalent in the US. Approximately 4.7 million Americans currently have Alzheimer's disease (AD) with an estimated growth to 13.8 million by 2050. An additional 3% to 22% of those over 60 years of age are thought to currently meet criteria for Mild Cognitive Impairment (MCI). The early detection of MCI and dementia is critical, as studies have shown that early pharmacological intervention may delay the progression of AD. Timely identification will become even more important once disease modification treatments are available. Unfortunately, most cognitively impaired patients do not seek early medical attention and physicians may not recognize subtle cognitive deficits during routine office visits. Patients typically present to their doctor 3 to 4 years after symptoms have begun. Furthermore, even practitioners aware of cognitive complaints may not perform a cognitive assessment, make a diagnosis or initiate medical interventions until at a later, more progressed stage of the disease. In fact, more than 40% of patients with mild dementia are not detected and diagnosed by their primary care physician. Use of sensitive and easily administered cognitive screening instruments is essential in overcoming the many obstacles encountered by physicians for early identification of MCI and dementia.

Online cognitive screening may provide early detection of cognitive impairment with the goals of directing these individuals to their physicians for evaluation and enhancing timely identification of pre-dementia research participants. However, online screening for cognition has been limited with mixed results. Although many excellent cognitive screening tests have been developed with good sensitivity and specificity for dementia recognition, most require an administrator and most are not available online.

The Self-Administered Gerocognitive Examination (SAGE) is a valid and reliable cognitive assessment tool used to identify both MCI and early dementia. SAGE's self-administered feature, pen and paper format, and four equivalent interchangeable forms allows it to be given in almost any setting, does not require any staff time to administer and makes it practical to rapidly screen large numbers of individuals in the community or in their home. SAGE consists of several parts. There are demographic questions, subjective questions, and objective cognitive testing.

In recent years, as more individuals gain access and become comfortable with the Internet, they are also accessing medical information online. Online retrieval of medical information can provide critical knowledge to consumers to improve their health. It may help them better understand their medical conditions or symptoms and potentially give them insight into ways to diagnose and treat their medical conditions. This information can be accessed anywhere they live in the world. In addition, there are websites that now offer health screenings including cognitive screening. The lay public has great interest and concern about their cognition and worry about developing neurodegenerative conditions like Alzheimer's disease. There are very few screening tests that target MCI. Having a validated online cognitive screening test may be very helpful for

individuals to identify their cognitive issues and have physician evaluation earlier than normally occurs. Individuals may also want routinely check their cognitive status annually through these online methods if validated. Since SAGE is self-administered, it could be an ideal tool to be used in a digital format online. The validity of SAGE in paper format had been studied and published (Scharre, 2010). We propose to study the validity of SAGE in a digital format for cognitive screening.

Study Objectives

Our objective is to validate SAGE in digital format (eSAGE) as a practical screening tool for detecting MCI and early dementia with a low false positive rate, by performing detailed neuropsychological testing on those individuals that did and did not make errors on eSAGE. We hypothesize that eSAGE will correlate well with gold standard neuropsychological testing designed to differentiate normal cognition from MCI and early dementia. We also hypothesize that the paper (SAGE) and electronic (eSAGE) versions of SAGE tested in a given individual will not show significantly different scores and will be correlated to each other to the extent that they could be used interchangeably.

Methods and Design

A. **Subject Selection**

1. Inclusion Criteria
   a. Adults over 49 years old of either gender
   b. Vision and hearing sufficient for compliance with tests
2. Exclusion Criteria
   a. Diagnosis by a physician of moderate or severe dementia
   b. Intellectual disability

B. **Method**

Subjects over 49 years of age with sufficient vision and English literacy will be recruited from a wide variety of community events including senior centers, health fairs, educational talks to lay public, independent and assisted living facilities, and free memory screens as well as from ambulatory Geriatric or Memory Disorders Clinics. The SAGE cognitive screening tool will be given to all subjects willing to take the test.

Participants who complete the SAGE test and meet inclusion and exclusion criteria will be divided into groups based on their initial SAGE scores. Each group will be composed of subjects with the same score. Individuals will be randomly selected from each group and asked to further participate in a one-time clinical evaluation. We will recruit approximately 5 subjects for each SAGE score from 10 to 22 at screening. Voluntary written informed consent and permission from the subject to interview a person who knows the subject well will be obtained. This could be a family member or a friend. Questions will be asked about the subject's cognitive and functioning abilities, known medical problems, and about any abnormal behavioral symptoms the patient may have. This interview may be telephonic. All efforts will be made to interview a close subject contact but this will not be exclusionary if no contact can be achieved.

The subject will be scheduled for one visit to complete the study. At that time the patient will be administered the outcome measures listed below, a medical history taken, and physical and neurological examinations performed including vital signs. The entire visit will take approximately 3 hours. There will be no cost to the patients to be included in this study. If

previously unknown significant abnormalities are found on any of these evaluations, the subject will be referred back to their primary care physician with a summary of the findings for consideration of further work-up with laboratory testing, neuroimaging, or other testing as deemed appropriate by their physician.

C. Outcome Measures

Cognitive Measures:

1. Paper version of SAGE (Scharre, 2010). Subjects will be given one of 4 versions (Forms 1, 2, 3, or 4) of SAGE.
2. Digital version of SAGE (eSAGE) (exactly the same questions and format as paper version except done on a computer). Subjects will be given the same version (Form 1, 2, 3, or 4) of SAGE but it will be in digital format (eSAGE).
3. Mini-Mental State Examination (MMSE) (Folstein, 1965)
4. Montreal Cognitive Assessment (MoCA) (Nasreddine, 2005)
5. Boston Naming Test (Kaplan, 1983)
6. Wisconsin Card Sort Task (WCST) (Berg, 1948)
7. Hopkins Verbal Learning Test (HVLT).
8. FAS verbal fluency task (Lezak, 1995)
9. Wechsler Adult Intelligence Scale III (WAIS III) Letter-number and block design subtests

Behavioral and Functional Measures:

1. Neuropsychiatric Inventory (NPI) (Cummings, 1994)
2. Activities of Daily Living (ADL) (Galasko, 1997; Lawton, 1969)

D. Outcomes/Results

Analysis will consist of comparing the subject's scores on the SAGE in digital and paper format to their neuropsychological test scores using correlational methods. False positive and false negative rates for eSAGE will be determined. We also want to compare the paper with the digital format of SAGE to determine if these two formats are equivalent to each other. We aim for 80% power with a two-tailed test conducted at 5% level of significance. A test of the null hypothesis of the (Spearman) correlation coefficient being 0.86 against the (lower) threshold of 0.75 for significant agreement would require 60 subjects. With 60 subjects we would have a power of 85%. So the proposed sample size of 72 subjects including 20% drop rate would provide enough power to validate the e-SAGE forms under the assumed research hypotheses in terms of agreement with the paper forms.

Risk-Benefit Analysis

The risks to the subjects are very low. The potential psychological risks would include any stress a subject may normally have in having a history, examination, and neuropsychological testing performed. The seriousness of this risk is very low.

The possible benefits of this study to the subject include the potential of early detection of cognitive impairments. The subjects will also be helping to validate a brief screening tool in digital format that may help detect MCI and early dementia in others.

Informed Consent

After subject eligibility for the study has been determined, informed consent will be obtained. If the individual is determined to not have the capacity to consent, assent will be obtained from the subject and consent will be obtained by the subject's legally authorized representative (LAR). Each subject and if required their LAR, shall read and sign the instrument of informed consent after having had an opportunity to discuss it with the participating physician before signing. The individual signing the informed consent will be informed that the subject can withdraw from the program at any time. Written informed consent is required prior to enrolling in the study. The signed consent form is kept at the physician's office. The consent form will be approved by the Institutional Review Board. It is the responsibility of the investigator to obtain consent and to provide the subject/LAR with a copy of the signed and dated consent form.

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