



DEPARTMENT OF
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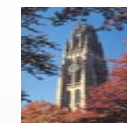


Efficacy of a Personalized Approach to Rehabilitation in Early to Moderate Alzheimer's disease

Jimmy Choi, PsyD,^{1,2} Paul Kirwin, MD,² Christopher H. van Dyck, MD,² Joanna M. Fiszdon, PhD,^{1,2}
Robert D. Kerns, PhD,^{1,2} & Morris D. Bell, PhD^{1,2}

¹ VA Connecticut Healthcare System, West Haven, CT

² Yale University School of Medicine, New Haven, CT



YALE UNIVERSITY
SCHOOL OF MEDICINE
Department of Psychiatry

Abstract

Introduction

Emerging literature calls for conjoint use of behavioral, neurocognitive, and pharmacologic treatments to enhance cognitive and functional outcome in individuals recently diagnosed with Alzheimer's disease (AD). For rehabilitation methods to be effective, patients must be motivated to participate. Participants with AD may have difficulty adhering to rehabilitation programs because of denial of memory deficits, general difficulty following through on daily tasks, and apathy, which may be primary to the illness or secondary to depression.

Purpose

Pilot study examines two novel rehabilitation approaches to improve cognitive and functional outcome in AD. Both approaches are designed to fully engage patient in treatment with motivational programs that are fun and enjoyable to do.

Primary research question is: Do patients with early to moderate AD benefit from cognitive training and a personalized rehabilitation program compared to treatment as usual?

Method

Pilot study is currently recruiting outpatients diagnosed with mild to moderate Alzheimer's disease who are on any AChEI regimen. Study uses a test, re-test treatment controlled design with participants randomly assigned to one of three 6-month conditions:

- o Treatment As Usual (TAU)
- o Computerized Cognitive Training (CCT), consisting of fun and engaging computer tasks of memory, attention, and problem-solving.
- o Personalized Approach to Rehabilitation (PAR), where in addition to existing pharmacologic regimen, patient is allowed to choose up to 3 of following components: computerized cognitive training, work therapy, supportive family psychotherapy, and/or a physical exercise/nutritional regimen. This approach is specifically intended to increase adherence to treatment by enhancing intrinsic motivation and empowering patients to be actively involved in treatment.

Assessments of cognitive function, quality of life, neuropsychiatric symptoms, activities of daily living, and treatment adherence are conducted at intake, 2, 4, 6, and 12 months.

Results

Study recruitment commenced in November 2006. Recruitment was initially slow due to screening out referrals who were in the moderate to severe range. Study currently has 9 active subjects with early to moderate cortical dementia, and a total recruitment goal of 60 participants by the end of 2008 (20 subjects in each research arm). Very early results on 7 subjects to complete 2-month follow-up show Computerized Cognitive Training group with general trend toward improvement in overall cognitive performance compared to Treatment As Usual. In addition, participants in the Personalized Approach to Rehabilitation who chose cognitive training, family therapy, and physical exercise showed greater treatment compliance, less depression and informant-reported psychiatric symptoms, and better quality of life compared to participants in the other conditions.

Conclusion

Current results are very preliminary with only basic statistical comparisons between groups on outcome measures. However, preliminary results convey that further exploration is worthwhile in developing specific and effective rehabilitative treatments designed to halt or delay onset of debilitating AD symptoms.

Background

Recent scientific evidence suggests concurrent pharmacologic and nonpharmacologic interventions may be better than medication alone in producing functional benefits in AD (van Dyck, 2004)

Available Nonpharmacologic Interventions

- Cognitive training has become widely available tool utilized in neuropsychiatric rehabilitation, including several recent empirical applications to early dementia intervention (Loewenstein et al., 2004)
- Physical exercise programs designed to keep patients physically active throughout progression of AD show moderate benefits in overall quality of life and reduction of medical comorbid conditions (Teri, Gibbons, & McCurry, 2003)
- Since most people with early AD live in the community supported by an identified primary caregiver, family/caregiver therapy to reduce tension, distress, and depression among caregivers may be beneficial to patient, as well (Davey et al., 2000)
- Work Therapy has shown to improve clinical outcomes in elderly psychiatric patients (Bell et al., 2005)

Problem

- Due to denial of memory deficits associated with AD, apathy, and behavioral symptoms, treatment noncompliance is a major concern in all aspects of their care (Clare et al., 2005)
- Increasing patient motivation for adherence by providing patients with treatment choices and a patient-determined treatment regimen has been associated with better outcome in neuropsychiatry (Choi & Medalia, 2005; Kern & Habib, 2004)

Hypotheses

For patients diagnosed with mild to moderate AD on a FDA-approved cholinesterase inhibitor:

- Does computerized cognitive training in conjunction with a cholinesterase inhibitor slow down the progression of AD
- Does computerized cognitive training enhance compliance to treatment as usual?
- Does the Personalized Approach to Rehabilitation show better outcome than computerized cognitive training alone or treatment as usual?
- Does the Personalized Approach to Rehabilitation promote greater adherence in rehabilitation, and therefore, better outcome?

Methods

Participants

- So far, participants enrolled are 9 elderly veterans at the VA Connecticut Healthcare System who met DSM-IV-TR criteria definition of Dementia of the Alzheimer's Type (DAT) according to assessment, medical chart review, and geropsychiatrist referral
- Psychometric differentiation of DAT from normal age-related cognitive decline or other memory disorders confirmed by Mattis Dementia Rating Scale (DRS) (Mattis, 1988)
- Inclusion Criteria:
 - DSM-IV-TR criteria for DAT, stabilized on AChEI for a minimum of 1 month, and psychometric criteria as follows:
 1. DRS age-corrected total cognitive profile based on the Mayo Older American Normative Studies (MOANS) (Lucas et al., 1998) for definition of Senile Dementia of the Alzheimer's Type (SDAT) will be equal to or below cutoff score of 122 on DRS Composite Score and 19 on DRS Memory subtest scores
 2. MMSE (Folstein M, Folstein S, & McHugh, 1975) score between 10 and 26 which is generally indicative of mild to moderate AD
 3. WRAT3 Reading Screen < 5th grade level to rule out developmental disabilities which may confound potential treatment effects (Jastak & Wilkinson, 1993)
 - Given the prevalence of clinical depression in dementia, depressive symptomatology carefully monitored throughout study using Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos et al., 1988)

Methods (cont'd)

	Baseline	Treatment As Usual (n=3)	Computerized Cognitive Training (n=4)	Personalized Approach to Rehabilitation (n=2)
Age		69 (2.78)	73 (4.24)	71 (2.11)
Education		11 (1.67)	12 (1.77)	10 (2.65)
DRS Composite		109 (10.71)	114 (4.67)	103 (5.44)*
DRS Memory Subtest		15 (1.20)	14 (2.40)	11 (1.60)*
ADAS-Cog (total errors)		22 (1.2)	29 (2.4)	36 (3.60)**
Folstein		19 (7.10)	18 (3.20)	14 (3.30)*
NPI		13 (4.06)	13 (6.42)	14 (3.20)
CSDD		9 (4.7)	10 (6.23)	8 (2.00)
QOL-AD		44 (4.45)	45 (6.70)	43 (4.50)
AChEIn/day		galantamine 24mg galantamine 12mg donepezil 5mg	donepezil 5mg donepezil 5mg donepezil 12mg	donepezil 10mg galantamine 24mg

Procedure

Randomized clinical trial using test, re-test treatment controlled design with recruited patients randomly assigned to control condition or two experimental conditions for approximately 6 months. Follow-up on all outcome measures at 2-months, 4-months, 6-months, and 12 months.

Interventions

Computerized Cognitive Training (CCT) uses a neuroscience-based cognitive rehabilitation program that incorporates repeated neurocognitive training exercises in patients with a variety of neuropsychiatric conditions. Modules provide comprehensive cognitive training program specifically designed for the elderly to increase participation in highly engaging but rigorous protocol which has been empirically shown to improve vital cognitive skills necessary for functional outcome (Merzenich et al., 2006, PNAS).

Treatment program involves repeated, computerized exercises in attention, memory and executive functioning within domain-specific training modules

Intervention includes at least twice a week, 45-minute sessions with facilitators providing tailored instruction and feedback to the patient as to encourage self-efficacy, intrinsic motivation, and proper execution of each training exercise.



Personalized Approach to Rehabilitation (PAR) is adapted from Alice Medalia's and Robert H. Kerns' innovative studies in patient motivation within context of schizophrenia and chronic pain treatment (Medalia et al., 2002; Kerns & Habib, 2004).

PAR incorporates a menu of treatment components that have each been empirically validated in neuropsychiatric rehabilitation. Approach is specifically intended to increase adherence to treatment by enhancing intrinsic motivation and empowering patients to be actively involved in their treatment

Patient is allowed to choose up to 3 components in addition to their existing pharmacologic regimen:

- o CCT consists of same treatment as noted above
- o Work Therapy is a highly supportive and structured therapeutic treatment which has been shown to improve work and clinical outcomes in elderly psychiatric patients. Patients work in supervised hospital work settings with sole intent of bolstering self-esteem and self-efficacy rather than vocational advancement (up to 8 hours/week for total maximum accrualment of 160 hours within 5 months)
- o Supportive Family Psychotherapy (1 session/week for about 5 months) consists of developing specific adaptive strategies for individuals and families dealing with early dementia as provided by an established family therapy protocol for use in elderly patients recently diagnosed with dementia (Mitselman et al., 2004)
- o Physical Exercise Regimen is a thorough physical exercise regimen in cardiovascular and aerobic exercise consisting of hourly training sessions about 2-3 times per week by physical therapists or physical therapist assistants for a total of about 25 session hours.

Preliminary Results

- To date, 7 subjects have completed 2-month follow-up
- No statistically significant difference in age, education, psychiatric symptoms, depression, and quality of life between groups at baseline
- PAR group seems to be more cognitively impaired on DRS, ADAS-Cog, and MMSE at baseline
- At 2-month follow-up, CCT shows trend toward better performance on ADAS-Cog compared to other groups
- CCT and PAR shows mild improvement in depression compared to TAU
- PAR shows less informant-reported psychiatric symptoms and better quality of life and treatment adherence compared to either TAU or CCT

Mean Change in Scores from Intake to 2-month follow-up	Treatment As Usual (n=3)	Computerized Cognitive Training (n=2)	Personalized Approach to Rehabilitation (n=2)
ADAS-Cog (total errors)	+1.11 (3.23)	-2.95 (1.79)	-0.14 (1.02)
Folstein	-2.34 (0.87)	+1.02 (1.00)	+1.55 (0.20)
NPI	+2.00 (2.34)	-1.06 (1.76)	-4.01 (3.20)*
CSDD	+0.75 (1.19)	-3.65 (2.23)*	-6.12 (3.03)*
QOL-AD	+2.66 (2.44)	+4.12 (3.23)	+6.92 (2.50)+
Appointments Made/Missed ratio	1.33	1.80	4.20*

* Mean Difference (Post Hoc: Tukey HSD multiple comparison) is significant at .05

Discussion

- Current results are very preliminary with only basic statistical comparisons between groups on outcome measures
- However, preliminary results convey promising trend for both interventions in attempts to halt or delay AD decline
- Rigorous cognitive training seems to have an impact on overall cognitive ability
- Results point to possible synergistic benefits of comprehensive, personalized rehabilitation program in conjunction with pharmacotherapy to enhance treatment adherence, psychiatric symptoms, and quality of life in AD compared to cognitive training alone or treatment as usual
- Protocol continues with ongoing recruitment and further follow-up assessments to gauge durability of current improvements

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