

What the Clinician Needs to Know about Reviewing the Cognitive Literature

Joshua Sandry, PhD

Neuropsychology & Neuroscience Research
Kessler Foundation

Department of Physical Medicine & Rehabilitation
Rutgers, New Jersey Medical School



jsandry@kesslerfoundation.org



Disclosures

No disclosures



Overview

- The Basics
- Evaluating the Literature
 - Inclusion Criteria
 - Methodology
 - Outcomes & Results
- Take away points

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The Basics

- The goal of Cognitive Rehabilitation Research:
To Determine Causal Efficacy of Treatment
 - Requires experimental methodology
 - Independent variable
 - Intervention
 - Dependent variable
 - Study outcome/endpoint
 - Impossible through correlational methods
 - Confounds
 - Hidden Variables
 - Directionality

The Basics

- Clinical Trial or Interventional Study

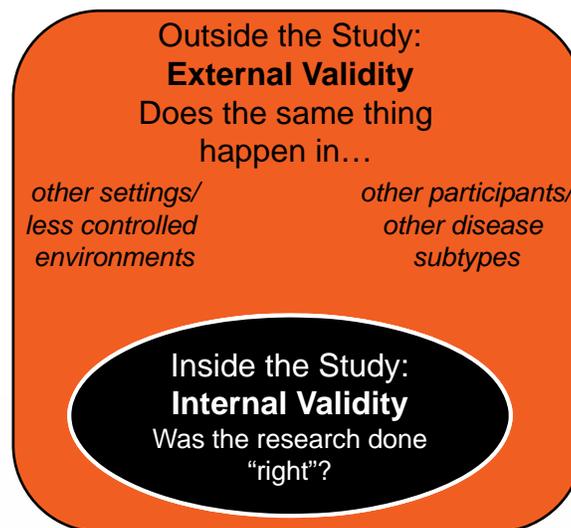
“...participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions.

- clinicaltrials.gov

The Basics

- Internal Validity – Methodological Soundness
 - How good is the evidence?
 - High internal validity = higher confidence in causality
 - Low internal validity = little to no confidence in causality
- External Validity – Generalizability
 - How well a study result can be generalized to other participants
 - Representativeness of sample to population

The Basics



The Basics

- Types of Cognitive Rehabilitation Interventions:
 - Restoration Approach
 - Designed to improve or alter cognition so that it operates similar to the efficiency it once was
 - Compensation Approach
 - Internal compensation strategy
 - Novel technique to learn, remember, organize or approach new information or situations, etc.
 - External compensation strategy
 - Use an outside device to learn, remember, organize or approach new information or situations, etc.

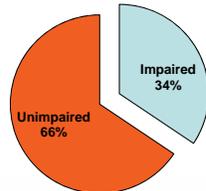
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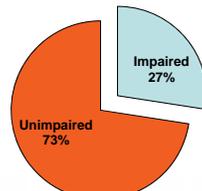
Evaluating the Literature

- Inclusion Criteria

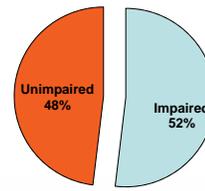
- All MS participants
- Mistakenly assumes all MS participants have cognitive impairment



CVLT-II DR



PASAT Total



SDMT

- Intervention efficacy or inefficacy may be masked by unimpaired MS participants. *May have missed it...*



Data from Benedict et al. (2006).
Impaired = ≤ 1.5 SD below healthy control



Evaluating the Literature

- Inclusion Criteria

- Clinician or Self-report vs Neuropsychological evaluation
 - Neurologist judgments
 - 49% of MS patients judged as cognitively intact were impaired (Peyser et al. 1980)
 - Patient self-report
 - 50% of MS participants are accurate at predicting their cognitive performance (Rosti-Otajärvi et al., 2014)
 - Less accuracy for more progressive cases (Rosti-Otajärvi et al., 2014)
 - Small/no relationships between subjective (self-report) and objective (neuropsychological evaluation) measures of
 - Memory (Bruce et al., 2010; Landro et al., 2000)
 - Processing speed (Roberg et al., 2012)
 - Somewhat better for executive functioning (Basso et al., 2008; Smith & Arnett, 2010; Van der Hiele et al., 2011)



Evaluating the Literature

- Inclusion Criteria
 - Clinician or Self-report vs Neuropsychological evaluation
 - Self-report measures may...
 - pick up psychiatric symptoms, e.g., depression or anxiety (Akbar et al., 2011; Benedict et al., 2004; Maor et al., 2001; Van der Hiele et al., 2011)
 - indicate MS participants' awareness of changes in their cognitive functioning (Christodoulou et al., 2005)

Evaluating the Literature

- Inclusion Criteria
 - Self-report vs Neuropsychological evaluation
 - **Scenario 1:**
 - Joe is a 52 yr old MS patient with memory complaints
 - Enrolled into a study to treat memory impairment based on self-report
 - He shows no benefit from treatment
 - Is the treatment ineffective?
 - Clinical testing
 - Psychiatric evaluation shows Joe is clinically depressed
 - Neuropsychological evaluation shows Joe is not memory impaired
 - Appropriate conclusion?

Evaluating the Literature

- Inclusion Criteria
 - What is general cognitive impairment?
 - Operationalized as impaired ≥ 2 cognitive measures
 - (PS & LTM) or (Att & EF) or (PS & ATT)
 - **Scenario:**
 - Participants enrolled based on “cognitive impairment”
 - Study designed to test novel executive functioning rehabilitation intervention
 - “cognitive impairment” as defined above allows participants w/o executive functioning deficits to be enrolled
 - Results - treatment does not “work”
 - Alternative explanation?
 - We can and should be more specific



Evaluating the Literature

- Inclusion Criteria
 - Participant Enrollment
 - Bias at the level of the group
 - People who volunteer may differ in motivation from those who do not volunteer
 - Less research on more progressive cases
 - Limited by mobility issues

Outside the Study:
External Validity

Inside the Study:
Internal Validity



Overview

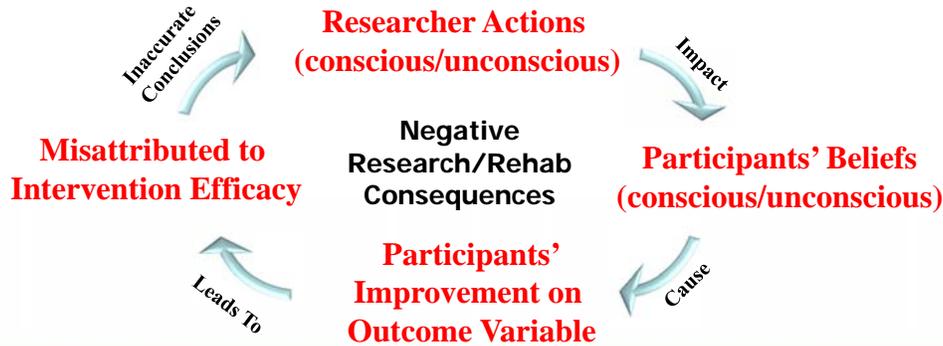
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Evaluating the Literature

- Methodology
 - Inadequate blinding
 - Rosenthal effect/Expectancy effects (Rosenthal, 1966/2002)
 - Researcher may unconsciously influence the outcome variable
 - Data/participants can be influenced by researchers expectations
 - Even nonverbal communication (reading from a script)

Evaluating the Literature

- Methodology
 - Inadequate blinding
 - Rosenthal effect/Expectancy effects (Rosenthal, 1966/2002)



Evaluating the Literature

- Methodology
 - Inadequate blinding
 - Treatment administration & Data coding
 - **Scenario:**
 - Researchers wish to test a therapeutic intervention designed to improve executive function and organizational abilities in MS participants
 - The intervention has to be administered by a therapist
 - The therapist may unknowingly and unintentionally influence the participant
 - Did the treatment work?

Evaluating the Literature

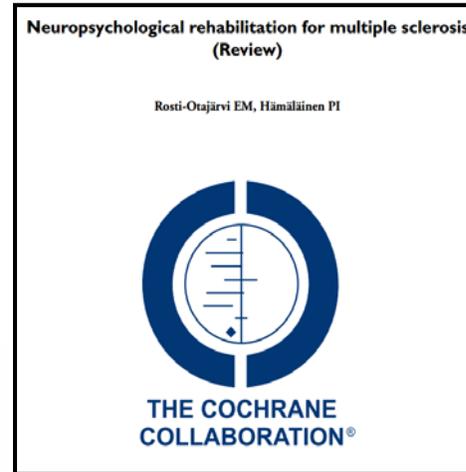
- Methodology
 - Control Groups
 - Wait-list/passive control groups
 - Easy to guess condition assignment
 - Practice effects
 - Compare against active control groups
 - “Active control groups are difficult and time consuming”
 - Difficulty should not preclude good practice in science
 - Strong designs allow for strong conclusions
 - Strong conclusions result in interventions that are most likely to help MS participants

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Evaluating the Literature

- Outcomes
 - 20 studies
 - 966 MS participants
 - **Findings:** Low-level evidence for rehabilitation
 - 18 of 20 in positive direction
 - Overall quality was low due to
 1. Methodological limitations
 2. Heterogeneous interventions
 3. Heterogeneous outcome measures
 - “well-designed, high quality studies are needed”



Evaluating the Literature

- Outcomes
 - “To draw firm conclusions that are based on systematic reviews that synthesize evidence from small numbers of randomized controlled trials of sometimes poor methodological quality, is undoubtedly overly simplistic” -Freeman & Playford (2012)
 - “The absence of evidence is not the evidence of absence” -Carl Sagan

Evaluating the Literature

- Outcomes

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

- *a priori* registered design/outcomes

- Compare the paper with the trial registration number
 - Transparent research practices
 - Making use of and reporting of all data and outcomes
 - Changing things halfway through

- HARKing (Kerr, 1998) **H**ypothesizing **A**fter **R**esults **K**nown
i
n
g



Evaluating the Literature

- Outcomes

- ▣ Different outcomes reported across studies

- Similar outcomes

2015
ANNUAL MEETING OF
MS
Assessment of Information
Processing Speed in Multiple
Sclerosis: Past and Future
Friday: 3:40 - 4:00 Room 103-104

- 157 articles
 - 64 different "processing speed tests"

Working
Memory/
Executive
Functions



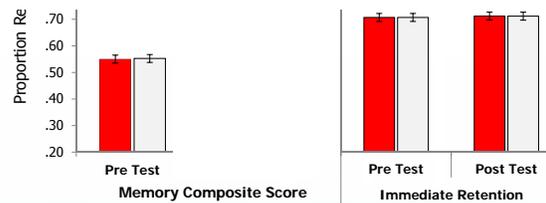
Data from Costa et al. (under review).



Evaluating the Literature

- Outcomes
 - Different outcomes reported across studies
 - Collapsing across tests
 - **Scenario**

$$\text{Memory Composite Score} = \frac{(\text{Immediate Retention} + \text{Delayed Retention})}{2}$$



Evaluating the Literature

- Outcomes
 - Functional neuroimaging results & interpretation
 - Some report increased functional activation after cognitive rehabilitation
 - Others report decreased functional activation after cognitive rehabilitation
 - Some consider changes adaptive while others consider changes maladaptive (Chiaravalloti et al., 2015)
 - Difficult to determine what changes in either direction may mean as an outcome
 - May be useful to consider these findings as descriptive

Evaluating the Literature

- Outcomes
 - Individual Differences
 - “Clearly, a key priority is to determine who benefits most from (and should receive) specific rehabilitation interventions.” (Freeman & Playford, 2012)



Evaluating the Literature

- Outcomes
 - Individual differences
 - Benefits of exploration...
 - Theory-driven
 - Apply models of cognition & cognitive neuroscience to understand heterogeneous cognitively impaired participants
 - Develop novel rehabilitation protocols
 - Pure exploratory
 - Interpret exploratory findings in light of existing models (post-hoc)
 - But say so...

**Keep HARKing
in mind**

Evaluating the Literature

- Outcomes
 - Individual differences
 - Impairment in one cognitive domain may be a result of cognitive deficits in another domain
 - Memory impaired MS participants enrolled in memory remediation program (Chiaravalloti et al., 2013)
 - Follow-up exploratory research
 - MS participants with processing speed deficits did not benefit as much from the remediation program compared to MS participants without processing speed deficits (Chiaravalloti & DeLuca, in press)



Evaluating the Literature

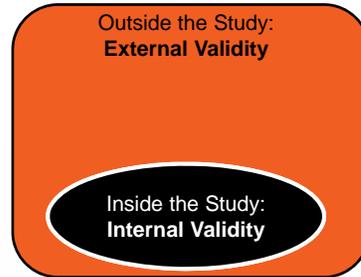
- Outcomes
 - Individual differences
 - Impairment in one cognitive domain may be a result of cognitive deficits in another domain
 - The appropriate course of action for cognitive rehabilitation may consist of multiple levels
 - First address one domain, reassess, then target another domain
- Example:** 1. resolve executive deficits
2. teach learning strategy to improve memory
- Patient-specific individual differences approach to cognitive rehabilitation* (Sandry, 2015, p.3)

Experimental tests of this hypothesis are necessary



Evaluating the Literature

- Generalizability of trial outcomes to daily life
 - Not many studies include everyday assessments of cognition
 - Not easy to measure everyday life
 - More on this in session 2 from Dr. Goverover



Evaluating the Literature

- Can I use “brain training” games?

A Consensus on the Brain Training Industry from the Scientific Community

Max-Planck-Institut für Bildungsforschung
Max Planck Institute for Human Development



October 20, 2014

75 Leading Cognitive Psychologists & Cognitive Neuroscientists
Representing 48 Universities

"In summary: We object to the claim that brain games offer consumers a scientifically grounded avenue to reduce or reverse cognitive decline when there is no compelling scientific evidence to date that they do.



"A Consensus on the Brain Training Industry... ", accessed (May 29, 2015),
<http://longevity3.stanford.edu/blog/2014/10/15/the-consensus-on-the-brain-training-industry-from-the-scientific-community/>



Evaluating the Literature

- Can I use “brain training” games?
 - No evidence to support brain training games for cognitive rehabilitation
 - More research is needed in cognitively impaired patients

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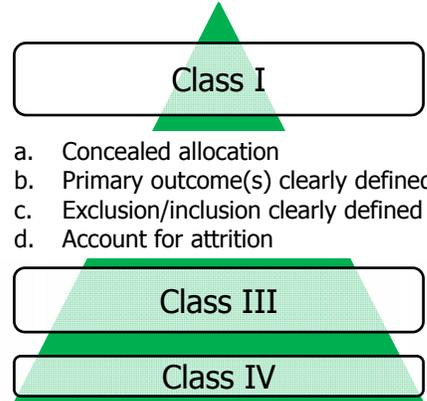
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Take Away Points

- What constitutes a good study?
 - Levels of evidence

CLASS I

Randomized clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. *As well as:*



Take Away Points

- What constitutes a good study?
 - Reviews that categorize studies based on criteria just covered
 - Systematic reviews
 - Meta-analyses
 - Fully evaluate the findings and use evidence-based approaches

Take Away Points

- Much of the cognitive rehabilitation literature suffers from serious design flaws
 - Cognitive impairment in MS is heterogeneous & cognitive rehabilitation treatments need to reflect these differences
 - Neuropsychological assessments should drive cognitive rehabilitation
 - Study conclusions need to match methodological limitations and avoid overreaching statements
 - Well-designed studies show cognitive rehabilitation can have a positive effect... *good vs. bad*
-

Conclusion

- Cognitive rehabilitation works and needs to be implemented - *DeLuca*
- Cognitive rehabilitation literature should be evaluated carefully – *Sandry*

So how do I do it the right way?

Cognitive Rehabilitation in MS: Part II

3:00 – 3:45

Innovative Assessments and Treatment
in MS: Practical Applications

Yael Goverover, PhD, OTR



3:45 – 4:30

Incorporating Evidence-based Approaches in
Treating Processing Speed and Memory
Deficits in MS into the Clinic

Nancy B. Moore, MA

