

# 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](mailto: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

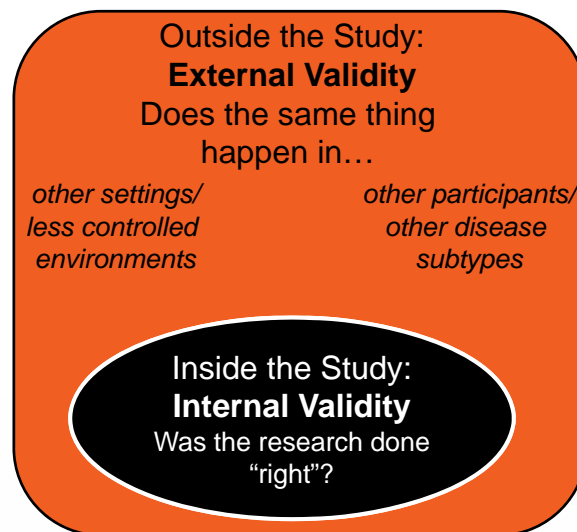
*“...participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic,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

- [clinicaltrials.gov](http://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.

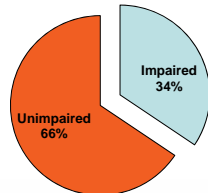
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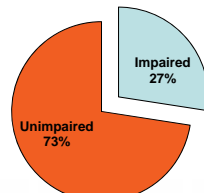
# Evaluating the Literature

- Inclusion Criteria

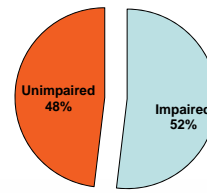
- All MS participants
- Mistakenly assumes all MS participants have cognitive impairment



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 =  $\leq 1.5$  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  $\geq 2$  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

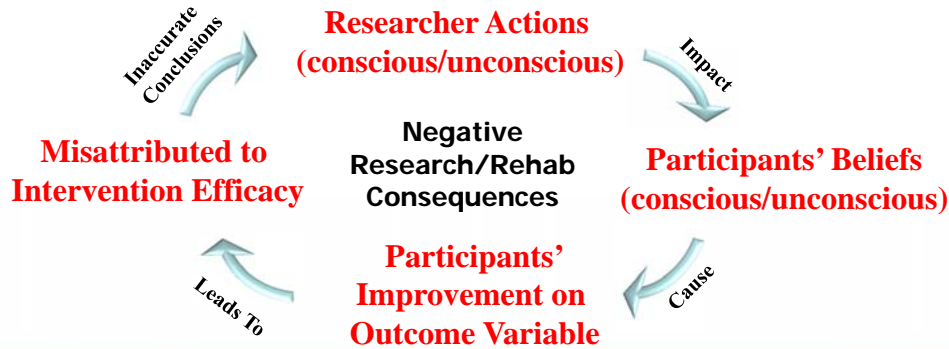
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## Evaluating the Literature

- 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

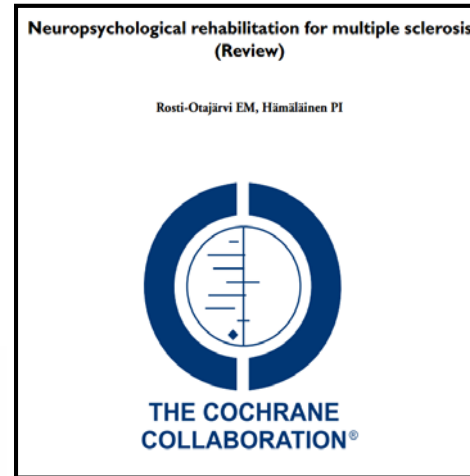
- Methodology
  - Control Groups
    - Wait-list/passive control groups
      - Easy to guess condition assignment
      - Practice effects
    - Compare against active control groups
      - “Active control groups are difficult and time consuming”
      - Difficulty should not preclude good practice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

## Overview

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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** y p o t h e s i z i n g  
**A** f t e r  
**R** e s u l t s  
**K** n o w n  
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"



Data from Costa et al. (under review).

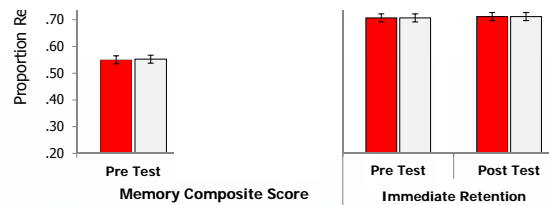


# Evaluating the Literature

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

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



# 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

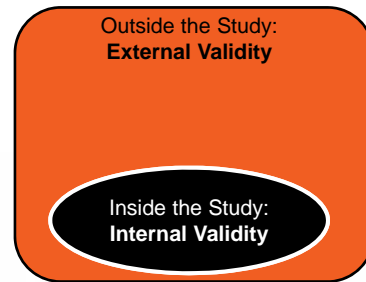
- Outcomes
    - Individual differences
    - Impairment in one cognitive domain may be a result of cognitive deficits in another domain
      - The appropriate course of action for cognitive rehabilitation may consist of multiple levels
        - First address one domain, reassess, then target another 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

## Overview

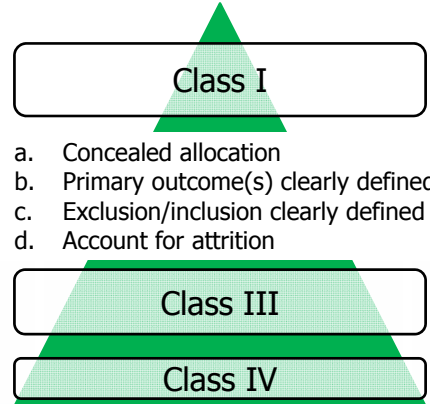
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# Take Away Points

- 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*

