Treatment Definition in Experience-Based Rehabilitation Research[1]

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Introduction

This paper addresses topics related to *defining and specifying treatments* in research on experience-based rehabilitation: that is, rehabilitation based in learning, structured practice/ experience, or deliberately designed interactions between therapist and participant.

Experience-based treatments introduce methodologic complexities compared to treatments that are expected to change the physical substrate passively, i.e., regardless of the behavior of the participant. For example, medications, surgeries and the application of certain devices may be considered passive treatments.

Although passive treatments have a place in rehabilitation, and in cognitive rehabilitation, researchers are also interested in treatments that are *active*, requiring cooperation and effort from the participant; and *interactive*, requiring specified behavior from the treater that is partly contingent on the participant's responses. *Environments* may also become a part of experience-based treatments—for example, when a phase of treatment involves practicing a task or skill in a noisy or distracting setting.

Defining an experimental experience-based treatment means specifying such matters as:

- **Who will do it**: i.e., treater characteristics such as training and experience; also, how treaters will be allocated across conditions
- **What will be done**: the specific activities and interactions contained in the treatment
- **How and when it will be done**: how often, for how long, at what schedule (intensity, duration and dose)
- **To what it will be compared** to estimate treatment effects: the control condition(s).

It seems obvious that these basic parameters must be specified in advance in order for treatments to be standardized and replicable. Yet treatment definition has been neglected relative to the exquisite detail with which we describe our participants and their deficits, and the care with which we select measures of treatment outcome (Whyte & Hart, 2003). In fact, one survey of treatment studies described in leading rehabilitation journals found that the majority of them did not describe treatments in sufficient detail for another researcher to replicate them (Dijkers et al., 2002).

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One way to ensure that you have adequately specified an experimental treatment is to *manualize* it.

Manualization

Manualization is a term borrowed from psychotherapy research, a field with decades of experience in specifying complex interventions based on therapist-patient interaction. Manualization ensures the level of detail that permits treatment to be carried out in the same way across participants, therapists, and clinical sites (in a multi-center study), to be replicated in future research, and to be generalized to clinical use.

Ideally, manualization occurs in 3 general steps or phases. (For the moment, we are only dealing with the experimental treatment; issues involved in the control condition are considered next.)

1. **Identify the active ingredient(s)** of your experimental treatment.
2. **Operationalize these ingredients** by specifying the therapist/ participant behaviors that should be associated with them.
3. **Translate these operations into a concrete product** (a manual = instructions and materials) that a therapist can use.

These steps can be quite difficult, both conceptually and practically. “Active ingredients,” for example, are easy to specify for medication trials (from which the term was borrowed) but not necessarily so for experience-based treatments. There are several reasons for this:

- There is no agreed-upon way that we articulate the mechanisms of action for learning-based treatments, in contrast to medications for which a chemical formula and pharmacokinetics may suffice.
- Experience-based treatments may be expected to have more than one active ingredient, especially if they are targeted to complex “real-world” problems, and/ or if they are based in interpersonal interactions. For example, so-called “common factors” such as the warmth of the therapist and his/ her ability to engage the patient, and the tendency of the patient to believe or not believe in the treatment/ therapist (and thus, to exert more or less effort), must always be considered in experience-based treatments. Such factors should be measured and controlled across conditions to the extent possible.

Rather than identifying all active ingredients with absolute certainty, the researcher usually must *hypothesize* the most critical mechanism(s) of action of interest to the study. This requires a relatively strong theoretical stance that will flow all the way through developing the protocol and manual including specifying the behavioral operations that support the hypothesis, and creating instructions that will emphasize the hypothesized mechanisms of action while downplaying others, or holding them constant.

Example

In the Table below, there is a simplified example of an experimental cognitive rehabilitation method and how its hypothesized active ingredients would be carried through each step of the manualization process. For this example, suppose that a researcher has reason to believe that a key problem-solving deficit in a certain type of brain injury involves "short circuiting" a normal sequential reasoning process. The researcher wants to test a treatment method called Fixed Sequence Problem Solving[2] that emphasizes sticking to the same general sequence of problem solving steps across many settings and types of problems.

Step	Example: Training in Fixed-Sequence Problem Solving
1. Identify active ingredients	Improvement in problem-solving will come about by applying a logical, sequential process in a fixed 4-step sequence: Identify problem, Generate Solutions, Select/ Implement, Evaluate/ Adjust. The more the participant adheres to this sequence, the more effective his/ her everyday problem-solving will be.
2. Operationalize with respect to therapist/ participant behavior	The therapist will explain the sequence, teach it to the participant, provide examples and guided practice, and assign and review homework. There will be major emphasis on the importance of using the sequence in a fixed way regardless of the problem or situation. The participant will learn the sequence using both explicit and implicit learning—s/he will be able to explain the sequence, will practice it in therapy sessions, and will apply it outside of therapy.
3. Translate into instructions and materials (manual)	The manual will include materials that explain the theoretical background of the treatment, emphasizing the importance of the fixed sequence. There will be instructions/ scripts on how to explain/ teach the fixed sequence to participants, and instructions on how to deal with common errors in applying it. Details will also be provided about the number of sessions, how long they are, and how to advance to more difficult materials depending on participant performance. Included will be practice problem-solving scenarios of increasing difficulty, instructions for how to use the participant's own problems in treatment, and instructions on how to assign and evaluate homework. All materials for both therapists and participant (homework forms, fidelity assessment forms, records of participant performance, visual aids/ handouts, etc.) are included in the manual.

[2] This is an invented example.

Problems and Issues in Manualization

In operationalizing the active ingredients of a treatment and translating operations into clinically relevant terms, the question arises as to how detailed the instructions to the therapist should be. Should a manual provide word-for-word scripts for the therapist to say to the participant and minute-by-minute instructions for what to do? If not, what type or level of guidance should be given? One of the pressing issues in manualization is the tension between *fidelity* and *flexibility*. Fidelity is the extent to which a therapist is "faithful" to the contents of the manual; flexibility is the extent to which treatment may be altered based on participant characteristics, response to treatment, etc. Unless the manual contains detailed algorithms for how the therapist is to be flexible in numerous possible situations, these two factors play off against each other in the actual implementation of a manualized intervention, and may be an important source of unplanned treater effects.

In determining how rigid vs. flexible to make the manual, the researcher must consider several factors that are summarized in the Table below. In brief, therapy operations may be specified in more detail the shorter the course of treatment, the narrower the focus of the intervention, and the more homogenous the sample population:

Study Parameter	LOW FLEXIBILITY	HIGH FLEXIBILITY
Target problem	Narrow; e.g., "working memory"	Broad; e.g., "memory compensations"
Sample population	Relatively homogenous	Relatively heterogeneous
Duration of treatment	Brief, e.g., one or several sessions	Longer, perhaps with an evolving or unpredictable course
Look and feel of manual	Scripts and detailed instructions	Tool kit of techniques linked by underlying theoretical orientation
Validation purpose	Internal validity	External validity

Actual treatment manuals are likely to have both types of components: fixed elements may be needed to make sure the hypothesized active ingredients are administered as planned; flexible elements may be needed for adjustment to individual participant characteristics. Also, as noted in the Table, therapy manuals may need to be less flexible to establish internal validity (efficacy), more flexible to establish external validity (effectiveness).

Selection and Definition of Control Conditions

As it is often challenging to define the experimental treatment, it follows that it may also be very difficult to select an appropriate control condition against which to test treatment effects. In the following discussion, based largely on Hart, Fann & Novack (in press), pros and cons of several types of control conditions are considered. In the discussion that follows it is assumed that participants are randomly assigned to one or another condition, as in a randomized controlled trial. However, many of the principles may be generalized to within-subjects designs such as crossover or multiple baseline designs.

The Placebo Problem

As a backdrop to the following discussion, the reader should keep in mind that although cognitive rehabilitation treatments are often referred to as having "placebo groups," it is almost never possible to create a true placebo for experience-based treatments. This is because of the essential elements of a placebo, as used in medication trials:

- it is harmless (placebo is Latin for "I will please")
- it is inert (inactive)
- it is identical, or nearly so, to the active treatment.

The resemblance to the active treatment is the basis for the placebo's very effective control for expectancy effects: that is, the participant's *and treater's* expectation of improvement. Such control is possible only because the placebo allows for double blinding. And double blinding is nearly impossible in experience-based trials—in fact, single blinding is difficult as well, since participants can most often figure out whether they are in the "more active" or "less active" treatment arm of a behaviorally based intervention (Whitehead, 2004).

Specific Control Conditions

Control conditions in which the treatment is withheld. The simplest form of control condition is one in which there is no attempt at placebo-- the treatment group is compared to another group that receives no treatment. The ***no-treatment control*** may be appropriate when it is ethically defensible[3] to withhold treatment and when there is no "gold standard" treatment for the disorder under study—conditions that are met by many if not most cognitive rehabilitation treatments. No-treatment conditions control for effects of time ("spontaneous recovery"), the effects of repeated testing, and regression to the mean, but *not* for expectancy effects. No-treatment groups may also lead to lower consent rates and/ or to disproportionate drop-out.

[3] Almost all discussions of the ethical issues involved in control groups assume that *some* treatment is better than *no* treatment. But experience-based treatments may be perceived as intrusive or demeaning, or they may perturb established family patterns in negative ways, or have other untoward effects at a higher rate than no-treatment conditions (Saks et al., 2002).

Some of these problems may be circumvented by using a group that begins the study with a no-treatment phase, but receives the treatment at a later time-- the so-called ***wait-list control***. This condition may be more palatable to participants, and may provide some control for expectancy effects. Wait-list controls have been used extensively in psychotherapy outcome research and have also been used effectively in cognitive rehabilitation trials (see for example Wilson, Emslie, Quirk and Evans, 2001). These control groups are not appropriate for trials of relatively long duration, or those with a long-term outcome evaluation. Under these circumstances, the protracted waiting period has the same disadvantages as a no-treatment group as well as adding the expense of tracking untreated participants over a long period of time.

Placebo analogue conditions. As noted above, attaining a "pure" placebo model in experience-based treatment is rare, but there are several control conditions that can give some of the advantages of a placebo. ***Sham treatment*** (also called ***pseudo*** or ***spurious treatment***) is a control method that provides a treatment theoretically irrelevant to the target problem. This is meant to control for expectancy effects and the effects of "common factors" associated with professional contact and attention. For example, memory training has been used as a control for problem-solving training, and vice versa (von Cramon, Matthes-von Cramon, & Mai, 1991; Schmitter-Edgecombe, Fahy, Whelan & Long, 1995). A sham treatment that consists of non-specific attention or stimulation has been termed ***attention control***. Sham and attention controls have the obvious drawback that they may not be credible to participants, especially those recruited into a study on the basis of having a specific problem which is then ignored. Credibility of treatment may be a more important factor in controlling for non-specific effects than time exposed to treaters or attention received (Whitehead, 2004). Sham treatments are also expensive, as they require two manuals, two sets of treaters or double the treatment time, etc. Another potential drawback of a sham treatment is that it may actually turn out to be effective for the target problem! Sham treatments, therefore, are best for testing strong, well-founded hypotheses about active ingredients.

Usual care comparisons. Experimental treatments that are attempting to improve on a standard of care may be compared to the "usual care" for the condition under study. A major advantage of this control is that it is credible and palatable to participants and treaters alike. However, it is not typically relevant for cognitive rehabilitation research, as there is unfortunately no (or highly inconsistent) usual care for cognitive problems. However, experimental treatments may sometimes be embedded in or superimposed on usual care interventions. For example, Geusgens and colleagues (2006) had Occupational Therapists implement a specially designed method for treating apraxia within the functional activities in their therapy sessions. Other patients (randomly assigned) received usual Occupational Therapy with standard training in functional activities. Both groups improved (*this outcome must be assumed in usual care comparisons*) but it could be shown that the special apraxia training led to better generalization on un-trained tasks. Another type of usual care design is known as ***devised usual care***, in which the researcher standardizes an alternative treatment that resembles a standard of care, but is hypothesized to be less effective than the experimental treatment.

Active treatment comparisons. As more becomes known about the efficacy of treatments, it is less important to compare them to *no* or *irrelevant* treatments, and more important to compare variations on one or more active ingredients. For example, ***dose control designs*** administer one or more weakened versions of an efficacious treatment to help establish the minimum dose necessary for beneficial effects. ***Dismantling designs*** compare "packages" of treatment ingredients that differ on one or more putatively active ingredients. ***Equivalence trials*** test the hypothesis that some new intervention is equivalently efficacious to an established treatment.

General Recommendations

1. To circumvent disproportionate drop-out, consider offering a brief, individualized treatment phase after the study is completed, to those who are randomized to the control condition.
2. Thoroughly document the *actual* amount and type of treatment for the target problem that is received by all participants both within and outside of the study protocol. Those in the control group (and the experimental group, for that matter) may be pursuing other interventions for the problem.
3. Explicitly measure the perceived credibility of all study interventions (experimental and control) as well as the expectation that participants will benefit from the trial.

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