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Single-Case Design in Psychophysiological Research. Part I: Context, Structure, and Techniques
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There is a growing consensus in the clinical literature about the importance of establishing and utilizing empirically supported treatments (ESTs). A number of established criteria for determining the efficacy and effectiveness levels of treatments are reviewed, and an argument is put forth that the research paradigm of large-scale group comparison designs may not be the best conceptual fit for studying psychophysiological phenomena. Clinical psychophysiology employs reinforcing successive approximations of functional abilities: a model closer in nature to operant conditioning, physical rehabilitation, and education than the standard pharmacological model. Single-case designs have a long, well-accepted history in scientific disciplines and require resources that allow practice-level clinicians to make meaningful contributions to the scientific literature. They also have a clear role in the establishment of a treatment as an EST. A discussion of the logic, structure, and techniques of single-case design is presented in sufficient detail to actively construct publishable studies. The adaptive nature of this technique makes it possible to address a wide range of potential psychophysiological research questions, along with barriers to utilization, including ethical considerations. Techniques are presented to allow researchers to examine treatment efficacy and effectiveness as well as isolate components of treatment to determine the most powerful elements of a clinical intervention.

INTRODUCTION: RESEARCH-BASED PRACTICE

Concurrent with a number of research protocols focusing on electroencephalography (EEG), a professional and theoretical shift is occurring in behavioral health, highlighting: the importance of evidenced-based treatment, the clinical utility of research, practicing clinicians accessing tools to contribute meaningfully to the scientific literature, and a growing focus on treatment efficacy and effectiveness (American Psychological Association [APA], 2002; Dupras & Ebbert, 2007; Glasgow, Lichtenstein, & Marcus, 2003; Johnson, 2008; Nash, McCrorry, Nicholson, & Andrasik, 2005).

A consensus is building around standards for empirically supported treatments (ESTs). This is an important, if not controversial, development in behavioral health because of the traditional scientist–practitioner split within the field (Spring et al., 2005). The scientist–practitioner split has not been an issue to the same extent within psychophysiology because of the technical nature of the treatment. The emphasis on ESTs has resulted in the formation of a number of task forces devoted to identifying standards of research (APA Presidential Task Force on Evidence-Based Practice, 2006; APA Task Force on Promotion and Dissemination of Psychological Procedures, 1995; APA Task Force on Psychological Intervention Guidelines, 1995). This, in turn, has led to the identification of much clearer standards to assess both the efficacy and effectiveness of specific clinical interventions.
The philosophical underpinnings and execution of these standards appear to be sound, and two of the leading psychophysiological professional associations, the Association for Applied Psychophysiology and Biofeedback and the Society for Neuronal Regulation, appointed a presidential task force to create a template for research standards that are yoked closely with the APA standards (La Vague et al., 2002; Moss & Gunkelman, 2002). Since the adoption of these standards, practitioners and researchers in neurotherapy and psychophysiology have established EST thresholds for specific interventions.

Thresholds include Level 1: Not Empirically Supported, Level 2: Possibly Efficacious, Level 3: Probably Efficacious, Level 4: Efficacious, and Level 5: Efficacious and Specific (Moss & Gunkelman, 2002). La Vague and colleagues (2002) detailed the criteria for each efficacy level. Level 1 (Not Empirically Supported) is designated to treatments supported by anecdotal reports and case studies in non-peer-reviewed journals. Level 2 (Possibly Efficacious) is designated to treatments supported by at least one study with adequate statistical power and well-identified outcome measures, although lacking random assignment to a control condition. Level 3 (Probably Efficacious) is designated to treatments supported by multiple observational studies, clinical studies, waitlist control studies, and within-subject and between-subject replication studies that produced beneficial results. Level 4 (Efficacious) is designated to treatments that meet the following criteria: (a) in comparison to a non-treatment control group, alternative treatment group, or sham (placebo) control employing random assignment, the active treatment is statistically significantly superior to the control condition or equivalent to an established treatment in a study with sufficient power to detect moderate differences; (b) treatment was conducted with a population treated for a specific problem, with inclusion criteria that are clearly defined and reliable; (c) valid and reliable outcome measures specific to the related problem treated are employed; (d) data are analyzed with appropriate statistical strategies; (e) diagnostic and treatment variables as well as procedures are clearly defined for replication by independent researchers; and (f) equivalence or superiority of the active treatment has been demonstrated in at least two independent settings. Level 5 (Efficacious and Specific) is designated to treatments that are statistically superior to a credible sham treatment, pill, or bona fide therapy in at least two independent studies. Following these standards, the Association for Applied Psychophysiology and Biofeedback published reviews of the efficacy of biofeedback and neurofeedback (Yucha & Gilbert, 2004; Yucha & Montgomery, 2008). However, these conclusions do not appear to be shared by the larger therapeutic community. For example, Division 12 of the APA (Society of Clinical Psychology) does not list a single neurotherapy application in their list of supported treatments and only “Biofeedback-Based Treatments for Insomnia” for psychophysiological interventions. This single listing is rated as having “Modest Research Support” (Society of Clinical Psychology, APA, Division 12, n.d.).

Further, in the case of Attention-Deficit/Hyperactivity Disorder (ADHD), which is one of the most widely researched applications in neurofeedback, with recent randomized control trials demonstrating efficacy and specificity (Arns, De Ridder, Strehl, Breteler, & Coenen, 2009, for a meta-analysis; Gevensleben, Holl, Albrecht, Schlamp, et al., 2009; Gevensleben, Holl, Albrecht, Vogel, et al., 2009), Division 53 of the APA (Society of Clinical Child and Adolescent Psychology) lists only Behavioral Parent Training, Behavioral Classroom Management, and Behavioral Peer Interventions as “Well Established.” There is no mention of EEG Neurofeedback or Neurotherapy. The same holds true for mood disorders, conduct disorder, oppositional behavior, and anxiety (Society of Clinical Child and Adolescent Psychology, APA, Division 53, n.d.). Similarly, clinical journal reviews for the treatment of autism contain no mention of psychophysiological interventions (Eldevick et al., 2009; Rogers & Vismara, 2008), although the
level of evidence for neurofeedback is “Level 2: Possibly Efficacious” with potential for Autism Spectrum Disorder (Coben, Linden, & Myers, 2010; Yucha & Montgomery, 2008).

Single-case design plays a vital, equivalent role in the establishment of an intervention as Empirically Supported. There are direct comparisons between single-case designs and group comparison designs. For example, the Society of Clinical Child and Adolescent Psychology and the Society of Clinical Psychology set their standards for inclusion as an EST in line with the emerging industry standards (Chambliss & Hollon, 1998). To be classified as a “well-established treatment,” at least two between-group design studies must show efficacy by revealing a superior treatment effect to placebo or other treatment, or an equivalent effect to an established treatment. A large series of single-case design experiments \( (n > 9) \) that shows efficacy with adequate experimental control and a superior treatment effect to other treatment may also be classified as well-established (Chambliss et al., 1998). Moreover, these between-group design and single-case design studies must utilize a treatment manual (a standardized, published document that specifies the rationale, assessment, and specific intervention procedures for a given treatment) and specify sample characteristics, with replication of the treatment effect by at least two independent research teams.

The second highest level of empirical support, or “probably efficacious treatments,” requires two studies demonstrating a statistically superior treatment effect to a waitlist control (manuals, sample specification, and replication by independent investigators are not required). One between-group design study demonstrating a superior treatment effect to placebo or other treatment, or an equivalent effect to an established treatment, also classifies as probably efficacious if it has clear specification of sample characteristics and utilizes a treatment manual. A small series of single-case design experiments \( (n > 3) \) is considered probably efficacious if showing a superior treatment effect to placebo or other treatment, with clear specification of sample characteristics, use of a treatment manual, and adequate experimental designs.

To assess the methodological power of a study, Nathan and Gorman (2002) outlined six types of studies. The most robust, Type 1 studies, require random assignment of treatment groups, specified inclusion–exclusion criteria, blinded assessments, cutting-edge diagnostic techniques, adequate sample sizes to power analyses, precisely defined statistical procedures, and treatment adherence measures. Type 2 studies require comparison of treatment groups; however, one or more aspects of Type 1 studies are missing (with the exception of critical design elements). Single-case design experiments are included in Type 2 studies. Type 3 studies have critical design elements missing, which include uncontrolled studies with pre–post designs and retrospective designs. Types 4 and 5 studies include secondary analysis articles. Type 6 studies include case reports.

**Internal Validity, External Validity, Efficacy, and Effectiveness**

Two of the primary research approaches in the clinical literature (efficacy and effectiveness studies) focus on related but separate issues. Efficacy studies focus on isolating all possible sources of variance: those that are known by stimulus control, sample matching, and anticipated confounding variables. For unknown confounding variables, random assignment and random selection are utilized to reduce systematic variances to statistical noise. Double-blind conditions and placebo control groups maximize the signal-to-noise ratio in detecting treatment effects. These studies must have adequate, often large, sample sizes to make the study sensitive enough to reduce the probability of Type I errors while maximizing the statistical power (or ability to detect differences between the groups when they in fact exist).

The next conceptual step is effectiveness studies. Once a clear cause-and-effect relationship has been established through controlled efficacy studies, effectiveness studies extend findings by focusing more on external validity: Do treatment effects generalize to real clinical
Clinicians often see individuals suffering with comorbid conditions and symptoms that do not fully meet criteria for a clinical diagnosis. Effectiveness research can examine issues that are directly germane to clinical practice, including client compliance and acceptance, generalizability across therapists, settings and geographic populations, treatment effect sizes, cost effectiveness, treatment feasibility, ease of dissemination, issues that affect treatment outcomes, and other real-world conditions (Chambless & Hollon, 1998; Chambless et al., 1996).

The purpose of efficacy studies is to maximize the internal validity: the degree to which treatment effects can be unambiguously attributed to the intervention. In essence, it is the clearest demonstration of cause and effect of the treatment variable. Efficacy studies do not necessarily inform practicing clinicians on technique, intervention, or mechanisms of action, but they do represent the "gold standard" for demonstrating that the treatment, and only the treatment, is responsible for therapeutic change.

Efficacy studies present significant problems for clinic or practitioner-based research:

1. They are extremely expensive. There are costs associated with subject recruitment, thorough assessment, skilled staffing to conduct the work, and equipment. The costs alone of doing this research are prohibitive for nearly all practice settings. To compound this difficulty, granting agencies, such as the National Institutes of Health, have devoted almost no funding for basic or applied psychophysiological treatment efficacy research. As a whole, practice-based research has received little attention from the National Institutes of Health (Westfall, Mold, & Fagnan, 2007).

2. Most sources cite a sample size of about 30 for each treatment condition (Kazdin & Bass, 1989), a subject pool size that is unlikely to happen except at the very largest treatment programs, and even then, self-presentation for treatment precludes random selection from a larger population.

3. Randomized assignment and treatment versus no-treatment or placebo control groups are functionally impossible in an applied clinical setting. The barriers are clear and well documented. Withholding of treatment or providing placebo treatment for an extended period is unethical in a clinical setting. In interventions that produce changes of physiological functioning with proprioceptive sequale, sham or placebo treatments are transparent (Tinius, 2005; Walker, 2010). Finally, random assignment is generally untenable in a treatment setting. In most cases, if the control group is an established treatment, the client ethically has to be given a choice, which is an act that, in and of itself, may pose a threat to internal validity but is necessary to conform to the standards of Informed Consent.

4. Despite these barriers, large group comparison studies are critical to establishing the efficacy of treatment. Without knowing with a high degree of certainty that the intervention is the primary causal factor in producing a significant outcome, further work (such as effectiveness studies) is diminished in its impact. In other words, studies that focus on efficacy and internal validity are necessary but not sufficient to demonstrate a particular approach is empirically supported.

In fact, some of the most pointed criticisms of psychophysiological interventions acknowledge the presence of well-conducted effectiveness studies but perceive that the psychophysiological literature contains an overfocus on external validity (effectiveness) before internal validity (efficacy) has been adequately established. According to Loo and Barkley (2005):

The reason we come back over and over again to scientific methodology is that proper experimental controls makes it possible to discern whether training EEG patterns is the active ingredient in the treatment. In fact, one of the biggest issues that the EEG biofeedback treatment literature needs to address is whether it is
actually the training of the EEG patterns that leads to improvement in ADHD symptoms. (p. 72)

IN SEARCH OF AN ACCURATE MODEL

Whereas some reviewers in the general literature have concluded that psychophysiology and neurotherapy are promising but unproven (Barkley, 2003; Gruzelier & Egner, 2005; La Vaque, 1999; Loo & Barkley, 2005; Nelson, 2003), others have been more dismissive (Lilienfeld, 2005; Lohr, Meunier, Parker, & Kline, 2001; Loo, 2003), and a host of ESTs have largely ignored the milieu altogether. However, practitioners and researchers familiar with the techniques and interventions cite robust effect sizes and effective treatment protocols (Hammond, 2007; Jensen, Grierson, Tracy-Smith, Bacigalupi, & Othmer, 2007; Lubar, Swartwood, Swartwood, & O’Donnell, 1995; Rossiter, 2004; see Yucha & Montgomery, 2008, for a review). Yet why is a disconnect present between biofeedback, neurotherapy, psychophysiology, and the larger literature?

A possible explanatory factor may lie not with the power, effectiveness, or specificity of the interventions themselves, but in the fact that the methods of investigation are based on models that are fundamentally wrong for the phenomena in question. Every field of scientific endeavor has its own methodological approach, and often studies in neurotherapy borrow methodological approaches that are rooted in medical and pharmacological traditions: using techniques that are appropriate to determining the efficacy of drugs (placebo controls, dose-response curves, randomized assignments, etc.). Further, reviews of the neurotherapy literature, from those in the field and from outside the field, reinforce those models by holding them up as a unitary standard (Arnold, 1995; Arns & Lyle, 2010; Heinrich, Gevensleben, & Strehl, 2007; Masterpasqua & Healey, 2003).

Greenberg and Newman (1996) maintained that multiple research approaches add to the literature and different approaches fit different problems. With careful examination of the studied phenomena, it is apparent that the pharmacological model may not be the best fit to assess the efficacy and effectiveness of neurofeedback. Both the techniques used and the goal of psychophysiological interventions hold closer similarities to other fields within the natural sciences.

The fundamental paradigm of neurofeedback, laid out by many of the leading researchers and practitioners (Egner & Sterman, 2006; Gunkelman & Johnstone, 2005; Malkowicz & Martinez, 2009), focuses on classical and operant shaping of a behavior toward an interstitial or terminal goal. The outcome is the measurable change of an organ or system (usually the central nervous system or autonomic nervous system) through the shaping process. The change of either the resting state or the ability to use the organ effectively in daily tasks is the clinical target. This is not a description of medication use. Rather, this is a description of physical therapy using behavioral techniques. Instead of focusing on a knee or a wrist, however, psychophysicologists are focusing on the nervous system.

Both applied behavior analysis and physical therapy are largely unquestioned in their overall effectiveness because they have developed, and journal editors have encouraged the publication of, methods that are appropriate to the field. They have encountered the same functional limitations and methodological challenges that neurotherapy and clinical psychophysiology now face. For example, physical therapy interventions, like psychophysiological interventions, often have transparency when attempting sham treatment or placebo treatment conditions.

Ultimately, there is no equivalent replacement for the traditional, large sample size, group comparison efficacy design. There are, however, research models and methods that are a good fit for clinical psychophysiology and neurotherapeutic techniques that can be implemented in clinical settings, even given the logistical and ethical constraints. The focus of the following section of this article is on the design and implementation of single-case designs in treatment-based settings, although
there are other good small sample size designs that have a high degree of scientific fidelity (Evans & Ilstad, 2001).

**SINGLE-CASE RESEARCH DESIGNS**

Single-case research designs (a bit of a misnomer, but the most widely used term for this model) are one of the behavioral scientists most powerful techniques. The fundamental concepts and procedures are well within the grasp of empirically minded practitioners. They can serve to communicate immediately usable clinical data through the scientific literature while helping build a body of referenceable work that demonstrates the potential and constraints of techniques. They have a deep history of scientific and clinical acceptance in addressing questions of efficacy, causality, effect size, clinical utility, cost-effectiveness, and cost–benefit ratios, all of which are listed as the critical components that contribute to Effective Practice (APA Presidential Task Force on Evidence Based Practice, 2006).

These techniques are not new (Skinner, 1933; Watson & Rayner, 1920), although they have seen a number of developments and refinements over the past two decades that made single-case interventions even more powerful, relevant, and accessible to clinicians in practice (Borckardt & Nash, 2002). Conceptual and analytical refinements have resulted in a consensus that well-constructed single-case design studies can produce powerful statements about both efficacy and effectiveness (Nock, Michel, & Photos, 2007).

In fact, Chambless and Hollon (1998), as an extension and refinement to the more general APA Task Force on Promotion and Dissemination of Psychological Procedures (1995), determined that a treatment can be designated “Efficacious” on single-case studies alone. No group comparison designs are even needed. According to the authors, a total sample size of three or more is required, with independent replication from a separate research site. Without independent replication, Possibly Efficacious, which is the designation for a number of industry-standard treatments (Rational Emotive Behavior Therapy + Exposure Therapy for Obsessive-Compulsive Disorder, Structured Psychodynamic Treatment for Posttraumatic Stress Disorder, Cognitive Therapy for Delusions in Schizophrenia; Chambless & Ollendick, 2001) can be demonstrated if there is no conflicting data. This standard has been adopted by many professional organizations including the Society of Clinical Child and Adolescent Psychology, Society for the Study of School Psychology, Society of Pediatric Psychology, Society for a Science of Clinical Psychology, the Association for Applied Psychophysiology and Biofeedback, and the International Society for Neurofeedback and Research (Moss & Gunkelman, 2002).

There continues to be much respect and acceptance for these techniques as the debate around empirically supported treatments become more sophisticated and refined. The APA Presidential Task Force on Evidence-Based Practice (2006) stated, “Single-case experimental designs are particularly useful for establishing causal relationships in the context of an individual” (p. 274). This does not rule out the importance of randomized controlled studies, which remain the most stringent way to evaluate efficacy within individual experiments (APA, 2002). Across multiple experiments, single-case design experiments are important both clinically and scientifically because they can be aggregated in a hierarchical fashion, providing a higher order level of analysis of treatment effects, in line with EST standards in many fields (Jenson, Clark, Kircher, & Kristjansson, 2007).

**BARRIERS TO UTILIZATION**

Blampied, Barabasz, and Barabasz (1996) and Barabasz, Barabasz, and Blampied (1996) published a thorough and highly readable summary of single-case research design techniques with special considerations specific to neurotherapy. Barlow, Blanchard, Hayes, and Epstein (1977) also published a review of these techniques specific to biofeedback. Despite laying a conceptual foundation in the literature, wide acceptance in the scientific community, and
tacit endorsement from the editorial board of these journals by publishing these articles, this model has not been widely utilized. The *Journal of Neurotherapy*, since its inception, has published very few articles using these research designs.

Given the ability of these techniques to drive the literature forward, demonstrate efficacy, and act as an effective conduit between clinical researchers and practitioners, why are they so underutilized? There is no easy answer, but research indicates that many professionals simply do not feel they have the training for these techniques. Clinical psychophysicologists come from diverse professional and theoretical backgrounds, and many professional training programs do not have specific coursework on single-case study designs. In fact, the utility of the model combined with its underutilization has led to it being called “counseling’s best kept secret” (Lundervold & Belwood, 2000).

Fundamentally, however, the techniques are not conceptually or logistically inaccessible to the practicing clinician. It would take a modest investment in time and study to understand the basic concepts and mechanisms of single-case designs well enough to put them in to practice. The reader is directed to Hayes (1981) for a review of the fundamental logic and design of the single-case design; Barlow et al. (1977) for a review of single-case design methods with an emphasis on psychophysiology; and Barabasz et al. (1996) for a primer on case studies and single-case design in neurotherapy, respectively.

Ultimately, the difficulty in conducting single-case design treatment research is likely a “devil in the details” situation of mastering not only the logic, concepts, and designs but also grappling with practical and ethical issues in a clinical setting. Some of the most common and the most difficult issues in conducting this research include (a) obtaining baseline data, (b) practical and ethical considerations of withdrawal phases, (c) obtaining simultaneous data for multiple baseline comparisons, and (d) techniques for empirical/statistical analyses.

The next section of this article presents a brief review of the basic elements of a single-case design and then addresses each one of the aforementioned issues to provide understanding, tactics, and techniques to allow clinical scientists to adapt research strategies to their own unique situations and studies.

**FUNDAMENTALS OF SINGLE-CASE DESIGN**

**Within-Series Approaches**

The foundation of the single-case design is comparing behavior across at least two conditions: a baseline and an intervention (Figure 1a). These two conditions are roughly analogous to the control and intervention groups in a classical group comparison design. If there is a change in behavior when the intervention is instituted, there is some evidence that the intervention may be the causal agent. Generally, studies that employ only a baseline, then an intervention, do not have enough rigor...
to definitively point to the intervention being the only source of the change in behavior (other causes may include maturation, incidental learning, placebo effects, etc.). To increase demonstration of the causal relationship, a reversal phase (the direction of reinforcement is reversed, i.e., bidirectional training) or a withdrawal phase (feedback or reinforcement is withdrawn completely) is employed (Figure 1b). If the behavior changes as a response, there is a much greater level of certainty that the intervention did indeed cause the observed change in behavior, by ruling out competing and confounding variables.

Obtaining Baseline Data. The most basic, and perhaps the most important, phase of a research-based treatment protocol is establishing the baseline. From the start, this presents challenges to clinicians who want to do research in a clinical setting. When patients come in with presenting complaints, they have a reasonable expectation of active treatment without undue delay.

Ethical considerations in the acquisition of baseline data may be dealt with in several ways. The primary ethical issue is obtaining data over multiple time periods without active intervention. However, there is a built-in opportunity for many psychophysiological applications to obtain baseline data without onerous delays in treatment.

The standard rule for baseline assessments is that at least three data points are required to establish the stability of the behavior or symptom being measured and to establish if there is a preexisting trend (Hayes, 1981). Three to five is recommended (Alberto & Troutman, 2006). If a more formal statistical analysis is planned, and for the purposes of publication or presentation, a minimum baseline of seven to 10 data points are required, with 15 to 20 or more being preferred (Borckardt & Nash, 2002).

In good clinical practice, a careful evaluation of psychophysiological, psychological, medical, and diagnostic considerations often preclude an immediate start to intervention. There are a number of methods for physiological assessment, ranging from full array Quantitative EEGs with Z score imaging to standardized approaches with clinician-level equipment, such as the MiniQ procedure (Swingle, 2008), to idiosyncratic practitioners’ preferred methods. All approaches include time spent gathering historical data, face-to-face interviews, and physiological baselines.

For example, it is not uncommon for electromyographic training to precede EEG interventions for several epochs before neurofeedback starts (Schwartz & Andrasik, 2003). If the EEG data are obtained during this training, and are sufficiently stable and trend-free over time, in a clinical setting they can be used as the A phase baseline data. The baseline retains its integrity especially well if plotted against the results of the electromyographic training to show independent effects (see simultaneous and alternating treatment designs next).

In psychophysiological research, there is no set rule that every epoch equals one session, or visit to the clinic. There may be several treatment conditions or data-recording sessions within a 1-hour visit. The key is consistency: All epochs must be functionally equal. If a quantitative analysis is planned or the case is eligible to be included in a multiple total sample size study (such as a multiple baseline), then these clinically appropriate data and rapport-building phases are a good time to collect epoch baseline data.

There will always be cases where the collection of baseline data is either ethically or practically unfeasible. Short baselines are preferable to no baseline, but neither condition is necessarily fatal to the parsimony of the design (Barlow & Hersen, 1984). Short or absent baseline conditions can be effectively addressed by utilizing a number of approaches, such as withdrawal conditions, between-series elements, and simultaneous and alternating treatment designs, or they may even be capitalized on by including them into a multiple baseline study as a comparison phase sequence. In clinical practice, perhaps the most actionable modification of a within-series design is to start treatment immediately, follow with a withdrawal condition, and end by reinstituting the
active treatment, or B/A/B design. Dealing with the withdrawal condition is addressed in the next section.

B/A/B Design. The B/A/B design is a variant of the traditional A/B/A design that is employed either as part of a planned multiple baseline design, or when there are ethical or practical limits on obtaining a baseline. The intervention is applied without delay, and when identified therapeutic targets are hit, treatment is withdrawn, but measurements are still taken, then treatment is reinstated. Internal validity is preserved to some extent by showing a trend to baseline during the withdrawal phase. Sulzer-Azaroff and Mayer (1977) recommended returns of only one third to two thirds of baseline levels to demonstrate efficacy. Alternatives are addressed in the next section if this criterion is not feasible. Because this design has no initial baseline, it is often considered weak, but it can be effectively integrated with other N=1 designs to great effect in a multiple baseline design as one of the baseline conditions.

Ethical and Practical Considerations of Withdrawal Phases. Richards, Taylor, Ramasamy, and Richards (1999) identified four primary situations in which the application of a B phase, or withdrawal condition, may be ethically problematic: (a) when the target is not reversible, (b) when the treatment effects will continue after the treatment is withdrawn, (c) when it is not educationally or clinically desirable for the behavior to return to near baseline levels, and (d) when the target behavior is such that withdrawal of treatment would be harmful or dangerous.

When dealing with clinical symptoms, it would appear that any withdrawal of clinical treatment would violate one of the four guidelines in nearly all cases, making negotiating the withdrawal phase one of the most difficult and confusing topics in clinical single-case design research. The difficulty of incorporating withdrawal phases has been cited as the single-case design’s greatest limitation (Bandura, 1969).

Beyond the ethical considerations, however, is the nature of clinical work itself. The expectation of the A/B/A model is that when treatment is withdrawn, the behavior will start to return to baseline levels. This presents a problem for many, if not most, clinical interventions, because the very nature of the treatment is to intervene in a way that the client continues toward an improved functional state. That is, the treatment effects generalize to the person’s life after the treatment is finished. The lack of a return to baseline, then, would indicate successful intervention, but also prevent demonstrating internal validity and the specificity of the treatment effect. Fortunately, deterioration of the target behavior is not required during the withdrawal phase (Sidman, 1960), but consideration about how to approach treatment generalization should be planned ahead (Barrios & Hartman, 1988).

The ethical and practical considerations are considered jointly because they are part and parcel to each other in the approaches that allow us to effectively address them. There are several approaches to maintain internal validity while minimizing risk to the patient. The first and most straightforward is to determine if a withdrawal phase would indeed be harmful.

As Hayes (1981) pointed out, there are often times of treatment withdrawal that are unplanned (therapist vacations, missed appointments, etc.) without incurring demonstrable harm. Data collection during this time (given the resources) is not prohibited but is not the same as a planned withdrawal, according both to Hayes and to Barlow and Hersen (1984). This would indicate, however, that planned breaks in the treatment may be ethically incorporated into a larger treatment protocol, not unlike the concept of drug holidays for patients determining the efficacy of medications. The limitation in a clinical setting is that these withdrawal periods are not blind, but the nature of single-case designs is that they do not necessarily call for blind or double-blind conditions.

If the ethical or practical limitations do rule out the use of a standard withdrawal phase, or treatment generalization would obfuscate the results, there are a number of practical alternatives that may be used, depending on the situation. These alternatives include
bidirectional training to increase mastery over the psychophysiological phenomenon at hand, adjustments in data analysis, using more sophisticated targets to measure during within-series designs, and utilizing between-series designs.

Managing Baseline and Withdrawal Phases by Measuring Rate of Change. There is an elegant but little known data analytic approach to the problem of demonstrating a therapeutic change with an intervention where effects are expected to continue after the treatment is withdrawn. The Periodic Treatment Effects approach utilizes the same modular treatment phases as a standard design and is particularly well suited to psychophysiological interventions.

When treatment is withdrawn (not reversed), physiological homeostatic forces will often settle around a new level of functioning. As a result, the slope, or rate of change, may tend to flatten when an active intervention is withdrawn. The periodic treatment effect approach can demonstrate both the efficacy and specificity of treatment by plotting not the raw data for each epoch (Figure 1a) but rather the rate of change between epochs (Figure 1b).

Calculating the change, or delta score, between sessions gives a clearer index of the change in functioning between epochs as well as the lack of change when treatment is withdrawn: Information that may be disguised by plotting raw data in conditions where treatment gains are expected to maintain (Hayes, 1981). Because of the autocorrelation nature of the data (addressed next), one must use caution when deciding to use a rate of change analysis (Jenson et al., 2007). In most cases, if the potential exists, a multiple-baseline design is preferred (Barlow & Hersen, 1984).

Another potential approach that is germane to psychophysiology is measuring the level of control an individual gains during treatment (Figure 2). This focuses not on second-order analysis (rate of change) but the amount of control demonstrated over the target system during each measurement epoch (Hayes, 1981). Clearly, if there is a specific treatment effect, an accurate feedback condition would produce within-epoch control greater than no feedback or sham feedback (Egner, Strawson, & Gruzelier, 2002). This may be calculated in a number of ways customized to the situation. A measurement may include the rate of improvement over one period (beginning values – ending values), the degree of specificity (muscle group relaxation vs. a reference muscle group or EEG bandwidth deflection), or a range of other clinically relevant targets. Focusing on the rate of control or mastery during treatment conditions, when compared to withdrawal conditions, is not only often more clinically relevant to psychophysiological intervention but more indicative of the treatment specificity. Moreover, because the initial parameters of psychophysiological measurement are variable from session to session, measuring the rate of change within a session often helps to stabilize trends that are difficult to differentiate when examining raw session data.

**BETWEEN-SERIES APPROACHES**

If the acquisition of a sufficient baseline is impossible, and the risk-to-benefit ratio does not warrant a withdrawal phase, there are still empirically valid ways to demonstrate internal validity by using the Between-Series strategy. These designs are effective when there are two or more conditions that are trained or two sites recorded simultaneously. In effect, they are the presentation of a B condition...
and a C condition (the underlying assumption is that they are functionally independent) in rapid succession so that one may be compared to the other, acting as a baseline and reference (Barlow & Hayes, 1979).

**Alternating Treatments Design**

One variant is the Alternating Treatments Design, which is based on rapidly alternating between two treatment foci. For example, if the treatment protocol calls for the alternating conditions of lowering then raising skin conductance or a specific EEG bandpass to train control of arousal states, these conditions could be randomly alternated and plotted simultaneously (Figure 3).

Because there are two conditions implemented at different times with independent measurements, this design may be conceptualized as a very rapid $A/B/A/B$ design (Campbell & Stanley, 1963). This approach is particularly amenable to psychophysiology because training in multiple systems, or the same system in different directions, is a common feature in many intervention protocols.

**Simultaneous Treatment Design**

Similarly, if a treatment protocol called for changing a feature of the subject’s EEG, such as theta/beta ratio at O1 (Swingle, 2008), a concurrent channel, placed distally, could be simultaneously recorded during the interventions. Demonstration of a significant change in one site with little to no change in a simultaneous independent site would add a measure of confidence to causal attributions to change brought by the intervention. Internal validity would be enhanced if a baseline were also obtained, making for an even stronger design $A/B + C$ (Figure 4).

There are a few key elements to consider that are common to both Alternating and Simultaneous Treatment Designs. For example, there is not a two-condition limit on alternating or simultaneous conditions. The treatments can be alternated within one treatment session, across different sessions, different times of day, and different days (Richards et al., 1999). The treatments should be counterbalanced in number, condition, and context (Alberto & Troutman, 1999), and there should be strong indications that the measures are independent of each other. Barlow and Hayes (1979) cautioned that multiple treatment conditions are not the same as a formal baseline because of the potential for treatment effect carryover.

**COMBINED-SERIES APPROACHES**

Combined-series strategies are used to make comparisons of both within and between a series of measurements.

**Multiple Baseline Design**

The multiple baseline design is one of the most commonly used combined-series approaches. It is favored due to its ability to control for artifacts of simple phase change ($A/B$) designs, such as history, maturation, recurring behavior, and practice effects (Hayes, 1981). Multiple baseline designs, or $N > 1$ studies, demonstrate the effect of treatment by showing changes
across multiple behaviors, individuals, or settings, when and only when the intervention is introduced. Varying the time at which the intervention is introduced (i.e., lagging the start of intervention across multiple behaviors or individuals) allows the clinician to determine whether the treatment is in fact influencing behavior change, or demonstrating cause and effect. Lagging A/B/C conditions with changes across different baselines independently demonstrates a cause-and-effect relationship (Figure 5).

Multiple baseline designs are particularly useful to clinicians as they are often treating individuals with comorbid symptomatology, or multiple physical symptoms associated with their reported problem. For example, when treating an individual with severe anxiety and stress, clinicians using biofeedback target the physical symptoms of anxiety, such as elevated levels of muscle tension, cold skin temperature in hands and feet, and restricted heart rate variability. Demonstration of a treatment effect requires significant change in only the targeted symptom (e.g., reduced muscle tension), whereas no change occurs in other symptoms until they have been treated. Figure 5 depicts the staggered treatment of cold temperature in the hands and feet of two individuals with severe anxiety using a traditional multiple baseline design. Here, a cause-and-effect relationship between biofeedback and increased skin temperature may be concluded given that the change in skin temperature occurred when, and only when, the intervention was introduced.

It is important to note that adaptive changes in one symptom have the potential to produce positive changes in other maladaptive symptoms due to generalization of the treatment effect. If this occurs, the clinician may simply test out the treatment effect by withdrawing the treatment and observing whether all of the maladaptive symptoms return. It may also be the case that during withdrawal, the individual’s symptoms settle around a new tonic resting state (Figure 5).

**CONCLUSIONS AND FUTURE DIRECTIONS**

Historically, medical and pharmacological models have been employed in psychophysiological efficacy research, with an emphasis on randomized controlled trials (RCTs). However, the behaviorally based single-case design has much to offer psychophysiology, as it answers the question: Is treatment efficacious and specific?

Chambless and colleagues (1998) and Chambless and Hollon (1998) clearly outlined the criteria for single-case designs to be classified as “well-established.” Single-case designs fit elegantly in to this paradigm. The highest level of criterion can even be demonstrated by this design strategy alone: a large series of single-case design experiments (n > 9) that are adequately designed (utilizing treatment manuals and specifying sample characteristics), showing a superior treatment effect.
when compared to an alternative treatment, and replicated by two independent research teams.

The authors hope that this article, written for clinicians and scientists, increases the likelihood that single-case design approaches will not only be a subject of further discussion and research in the field of applied psychophysiology, but also will be pursued by clinicians in the service of providing empirically based interventions that enhance their clients’ well-being. Although RCTs are without a doubt an important part of determining treatment efficacy, single-case designs will successfully allow clinicians, who are often logistically unable to participate in RCTs, to engage in meaningful research that contributes to the psychophysiological literature.

REFERENCES


