DESIGNING MORE EFFECTIVE BEHAVIORAL INTERVENTIONS: USING THE ORBIT MODEL FOR BEHAVIORAL INTERVENTION DEVELOPMENT

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Changing unhealthy behaviors is the “single greatest opportunity to reduce premature deaths…”

Estimates are that 50% of new cancer cases could be eliminated through engagement in healthy behaviors

- Smoking cessation
- Physical activity
- Healthy diets
- Weight management
- Regular screenings
Improving health-related behaviors can have powerful effects on health …

A 7% weight reduction and 2.5 hour per week activity increase led to a 58% reduction in the cumulative incidence of Type 2 diabetes in older insulin-resistant individuals (Diabetes Prevention Program Research Group, 2002).
Trials of Hypertension Prevention II: Weight loss over 36 months in 2382 overweight pre-hypertensives

But even when behavior change is successful, maintenance of healthy behaviors across time is challenging.
The Challenge: How can we design more effective health-related behavior change interventions?

In biomedical research, a well-defined translational process exists that guides the development of new basic biological discoveries into efficacious therapies.

Building better behavioral interventions depends on defining a similar process to accelerate the translation of basic behavioral science research into more effective behavioral interventions.
Basic science discoveries used to develop new treatments

Testing use of proven therapies in clinical practice & community settings

T1 Translation

T2 Translation

The whole point of the research enterprise
Basic research discoveries used to develop new treatments

Testing use of proven therapies in clinical practice & community settings

The whole point of the research enterprise

Basic Research
Discovery
Mechanisms
Associations

Intervention Development

Dissemination & Implementation

Efficacy Trials

T1 Translation
T2 Translation

bBSSR
Behavioral Interventions
Public Health
Many findings from basic behavioral & social sciences research are ripe for translation into intervention

- We are seeing a rapid expansion of knowledge in the basic behavioral & social sciences in a variety of fields:
  - Behavioral neuroscience
  - Communication science and social marketing
  - Executive functions (memory, planning, inhibitory control)
  - Affective, motivational and social processes
  - Choice & decision-making
  - The psychophysiology of stress
  - The dynamics of social systems

- New basic behavioral science discoveries are leading to important new insights about behavior & behavior change
Basic, interventional & clinical/community behavioral research: a continuum or parallel play?

Basic behavioral & social science research

Behavioral & psychosocial intervention studies

Public health & community interventions

T1

T2
Challenges in Translation I behavioral science

Findings from cutting-edge basic behavioral science discoveries are often underutilized in the design & testing of health behavior change interventions due to:

- **no widely accepted framework** to describe behavioral translation I/behavioral intervention development (as is true for drug development research)

- **lack of industry support** for health behavior intervention development (no equivalent to the pharmaceutical industry);

- **few NIH funding opportunities**, no training opportunities, review groups not set up to review translation I/behavioral intervention development

- **few incentives** to create & maintain interdisciplinary teams required to conduct translational research;

- **lack of academic recognition** for bridging basic-clinical fields of study; and

- **high-risk nature** of translational and intervention development research
Obesity Related Behavioral Intervention Trials (ORBIT) RFA program

- **Objective:** To translate findings from basic research on human behavior to develop more effective interventions to reduce obesity & improve obesity-related health behaviors

- **Mechanism:**
  - Trans-NIH U01 (Cooperative agreement)
  - Supported by NHLBI, NCI, NIDDK, NICHD, OBSSR
  - 7 ORBIT research sites & 1 Resource & Coordination Unit (RCU)

- Each research center supports interdisciplinary project teams of basic and applied biological, clinical, behavioral and social scientists who are developing novel obesity-related interventions through formative & experimental research, early phase trials & pilot studies
ORBIT Projects

SCALE: Small Changes and Lasting Effects (NHLBI) Mary E. Charlson, M.D., Weill Medical College of Cornell University, NYC

Translating Habituation Research to Interventions for Pediatric Obesity (NIDDK) Leonard H. Epstein, Ph.D., SUNY at Buffalo, NY

Novel Interventions to Reduce Stress-induced Non-homeostatic Eating (NHLBI) Elissa Epel, Ph.D., Barbara Laraia, Ph.D., Nancy Adler, Ph.D., UCSF, CA

Increasing Sleep Duration: A Novel Approach to Weight Control (NCI) Rena Wing, Ph.D., Miriam Hospital, Providence, R.I

Habitual & Neurocognitive Processes in Adolescent Obesity Prevention (NHLBI & NICHD) Kim Daniel Reynolds, Ph.D., Claremont Graduate University, CA

Developing an Intervention to Prevent Visceral Fat in Premenopausal Women (NHLBI) Lynda Powell, Ph.D., Rush University Medical Center, Chicago, IL

Interventionist Procedures for Adherence to Weight Loss Recommendations in Black Adolescents (NHLBI & NICHD) Sylvie Naar-King, Ph.D. & Kai-Lin Catherine Jen, Ph.D., Wayne State University, Detroit, MI

Resource and Coordination Unit (RCU) (OBSSR) David Cella, Ph.D., Northwestern University, Chicago, IL

National Institutes of Health S. Czajkowksi (NHLBI/NCI), J. Boyington, S. Arteaga, P. Kaufmann, C. Stoney, M. Stylianou (NHLBI); F. Perna, L. Nebeling (NCI); C. Hunter (NIDDK); D. Olster, W. Smith (OBSSR); L. Haverkoss, L. Esposito (NICHD)
Translating Ideas into Interventions: The Process of Developing Behavioral Interventions
NIH-sponsored Workshop
December 6-7, 2010

- What model or framework can we use to guide the behavioral intervention development process?

- Which study designs & methods are most appropriate for the development of behavioral interventions?

- How do we create environments that foster creativity & encourage the development of innovative behavioral interventions?
Why do we need a framework to guide behavioral intervention development?

- The drug development model, while not without flaws, has resulted in the creation & testing of many life-saving and life-extending treatments.

- Use of a framework and identification of well-defined and appropriate methods in behavioral intervention development research can:
  
  - Accelerate the flow & development of new, innovative approaches to changing behavior from basic studies of human behavior to efficacious interventions.
  
  - Encourage the development of behavioral interventions that are well-characterized, appropriately tested & optimized prior to testing in larger, more expensive Phase III trials – ultimately leading to better, more powerful behavioral interventions.
  
  - Identify “failures” earlier in the process, allowing for refinement of interventions and reducing premature testing of “weak” behavioral interventions in Phase III trials.
The drug development process

- **Phase 1**: Laboratory and animal studies
  - Subjects: 20-100 Healthy volunteers
  - Purpose: Assess safety & biological activity
  - Time Course: Year 1-2
  - New Drugs Passed: 100%
  - 70% of INDs

- **Phase 2**: 100-300 Patient volunteers
  - Purpose: Determine safety & dosage
  - Time Course: Year 3
  - INDs: 33%

- **Phase 3**: 1,000-3,000 Patient volunteers
  - Purpose: Evaluate effectiveness & side effects
  - Time Course: Year 4-5
  - INDs: 27%

- **Purpose**: Verify effectiveness & monitor adverse long-term use
  - Time Course: Year 6-8
  - INDs: 0%
<table>
<thead>
<tr>
<th>Model/framework</th>
<th>Primary focus</th>
<th>Level of detail</th>
<th>Translational Phases Included</th>
<th>Consistent w/ drug development process?</th>
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<tbody>
<tr>
<td>ORBIT model</td>
<td>2-phase model for developing behavioral interventions w/ a focus on preventing &amp; treating chronic physical diseases</td>
<td>--IDs clinically significant target(s), cutpoints, milestones --provides examples of methods, bi-directional --ID’ing mechanisms of action not essential</td>
<td>Focuses on pre-efficacy phases (Phases I &amp; II)</td>
<td>Yes – uses similar phases, terminology</td>
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<td>Greenwald &amp; Cullen (1985)</td>
<td>5-stage model to guide cancer control research</td>
<td>--does not include ID of clinically significant targets, cutpoints, milestones --does not define all steps needed, designs/methods</td>
<td>Includes all phases from hypothesis development (Phase I) through D &amp; I (Phase V) research</td>
<td>Yes – uses similar phases, terminology</td>
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<td>Flay, 1986</td>
<td>8-phase framework for development of health promotion programs</td>
<td>--does not include ID of clinically significant targets, cutpoints, milestones --does not describe designs/methods --not bi-directional</td>
<td>Includes all phases from basic research (Phase I) through Demonstration studies (Phase VIII)</td>
<td>Uses similar terms (e.g. “phases”), but different meaning (e.g., Phase V = efficacy trials)</td>
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<td>Rounsaville et al. (2001); Onken et al. (2014) Stage Model</td>
<td>3-stage model, updated in 2014 to include 5-stages, w/ a focus on developing psychological treatments for mental health, substance use/abuse disorders</td>
<td>--does not include ID of clinically significant targets &amp; cutpoints --does include milestones, methods, bi-directionality --emphasis on ID’ing mechanisms in each stage</td>
<td>Includes all phases from basic research (Stage 0) to D &amp; I (Stage V)</td>
<td>No – “stages” not “phases” with different meanings (e.g., “Stage I” = intervention development, “Stage II” = efficacy testing)</td>
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<td>Medical Research Council (MRC), 2008</td>
<td>Proposes a 4-phase cyclical framework for developing &amp; evaluating complex interventions</td>
<td>--does not include ID of clinically significant targets, cutpoints, milestones, all steps in intervention development --does include example methods, bi-directionality</td>
<td>Includes all phases from intervention development through Implementation</td>
<td>No – not consistent w/ biomedical model (e.g., 3rd phase – “Evaluation” – assesses effectiveness &amp; cost-effectiveness)</td>
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The ORBIT Model for Behavioral Intervention Development

The ORBIT Model for Behavioral Intervention Development

1. **Basic Behavioral and Social Sciences Research**
2. **Significant Clinical Question**
3. **PHASE I**
   - **Design**
   - **Define**
   - **Refine**
4. **PHASE II**
   - **Proof-of-Concept**
   - **Pilots**
5. **PHASE III**
   - **Efficacy Trial**
6. **PHASE IV**
   - **Effectiveness Research**

**Optimization**
SIGNIFICANT CLINICAL QUESTION

Begin with a health issue that poses a significant problem

-- A disease that is increasing in numbers, severity, exclusively affects or is increasing in a subgroup

-- A health problem for which no treatment exists, or treatment is not very effective (could be optimized)

-- Requires a new approach to improve outcomes

-- Involves a novel risk factor or new approach to treatment
Improving Obesity-Related Behaviors: A Significant Clinical & Public Health Problem

In the U.S., obesity has risen at an epidemic rate over the past several decades.

2/3 of U.S. adults & 1/3 of children are either overweight or obese.

Overweight & obesity increases risk for cancer & other chronic conditions such as diabetes, heart disease, stroke.
The ORBIT Model for Behavioral Intervention Development
Neuroscience & Eating Behavior

Mesolimbic Reward Pathway
- The “pleasure center”
  Sex, Food, Drugs, Gambling
- Impulsivity/Immediate Gratification
- Overrides the homeostatic energy system e.g. “Always room for dessert!”

Prefrontal Cortex: Executive Function
The “CEO” of your brain
- High-level decision-making
- Planning
- Self-Monitoring
- Pursuing goals
- Delaying gratification
- Behavioral inhibition

Implications for Weight Loss Interventions:
- Avoid Triggering the Limbic Reward Circuit: Remove temptations from the home
- Enhance Executive Function: Training in Inhibitory Control, Self-Management Skills, Planning
The ORBIT Model for Behavioral Intervention Development

Basic Behavioral and Social Sciences Research

Significant Clinical Question

(a) Define

(b) Refine

PHASE I
DESIGN

PHASE II
PRELIMINARY TESTING

(a) Proof-of-Concept

(b) Pilots

Efficacy Trial

PHASE III
EFFECTICACY

PHASE IV
EFFECTIVENESS

OPTIMIZATION
Phases of Behavioral Treatment Development: ORBIT Model

**Phase I: Design**

Phase Ia -- *Define* the scientific foundation & basic treatment elements

- Identify behavioral risk factor target & clinically significant milestones
- Provide basic behavioral & social science research basis for treatment components & targets
- Identify candidate intervention components
- Describe pathways through which treatment can affect outcomes

**Study Designs & Methods:**

- Laboratory & field experiments to identify behavioral & biological mechanisms of action
- Observational studies to identify key intervention targets & points of “entry”
- Qualitative & mixed methods research to assess acceptability of proposed approach to end-users – “user-centered” research
Phase 1a: Define Hypothesized Pathway

**Behavioral Treatment**

- Multi-Component Intervention
  - Reduce Triggers
  - Mobilize Executive Function

**Treatment Targets**

- ↑ Environmental Rearrangement
- ↑ Goal Setting Skills
- ↑ Planning Skills

**Behavioral Risk Factor**

- ↑ Physical Activity (150 min/wk)

**Clinical Endpoint**

- ↓ Weight (>7%)
Unhealthy dietary habits may be initiated by a cue that is linked to the eating behaviors in memory.

- Aim of the intervention was identify & disrupt these unhealthy cue-behavior links and create new and stronger links for healthy alternatives.

In Phase Ia, Ecological Momentary Assessment (EMA) was used to identify physical, social, and intrapersonal cues that were associated with the consumption of sweetened beverages and sweet and salty snacks in 158 low-income adolescents.

Answered brief surveys via PDA’s about their eating behaviors (location, social environment, mood, stress, and food cravings, drink, snack, and meal time items consumed) over 7 days -- each time they ate or drank something, when randomly prompted by the PDA, and once each evening.

Identification of these cue-food links allowed development of an intervention designed to substitute a different behavior when the relevant food “cue” was encountered.
For treatment of obesity, the goal of all dietary prescriptions is to reduce energy intake.

- Energy-dense, non-nutrient-dense foods are commonly targeted for reduction.
- Adherence to reduced energy intake is challenging, and novel approaches that enhance satiation during treatment of obesity are needed.

Habituation theory -- repeated presentation of a stimulus influences responding to the stimulus.

- Eating involves the repeated presentation of food stimuli (visual, olfactory, and gustatory stimuli), both within and across eating occasions.
- Habituation is demonstrated by a reduction in physiological and behavioral responses to repeated presentation of a stimulus.
- Hastening the rate of reduction should decrease the length of an eating occasion (enhancing satiation), reducing food intake.

Can a limited dietary variety prescription be developed that harnesses the effects of habituation on satiation and can be implemented within an intervention?
Salivation changes across trials - Group 1

Responses for food - Group 1

Epstein et al, 2009
The ORBIT Model for Behavioral Intervention Development
Phases of Behavioral Treatment Development: ORBIT Model

**Phase I: Design**

Phase Ib – **Refine** the intervention for strength & efficiency
- Identify essential treatment components
- Determine aspects of delivery (mode, frequency, duration, dose, intensity)
- Determine need for tailoring (e.g., for subgroups)

**Study Designs & Methods:**
- Small-N, case series &/or experimental studies that test effects of varying an intervention’s content, timing, frequency, duration, intensity & mode of delivery (“dose-finding”) and describe dose-response relationships
- Novel methods for developing, testing & refining behavioral interventions such as Multiphase Optimization Strategy (MOST) & adaptive treatment (SMART) designs
Habituation & Food Intake: Phase Ib: Refining intervention content
Epstein et al, 2010
Habituation & Food Intake:
Phase Ib: Refining intervention content
African American Adolescents ages 12-16 with BMI ≥ 95 percentile & primary caregiver

Examined potential moderators of weight loss treatment effects

Better executive functioning (EF) was associated with more weight loss

Suggests tailoring of weight loss interventions to address EF problems may enhance outcomes
Phases of Behavioral Treatment Development: ORBIT Model

**Phase II: Preliminary Testing**

Phase IIa – *Proof-of-Concept Studies*
- Determine if the intervention can achieve a *clinically significant signal* on the relevant behavioral risk factor
- Inexpensive initial test of a fixed protocol

**Study Designs & Methods**
- Typically non-randomized
- No control group
- Small-N, single-case designs
Behavioral Control of Overeating

Stuart, R.B., 1967
Phase 2a: Proof-of-Concept

ELM
(N=29)

Goal: <50% with High-Risk Waist Circumference

Percent with High-Risk Waist

Months in Study

45% at goal
The ORBIT Model for Behavioral Intervention Development
Phase II: Preliminary Testing

Phase IIb –

- **Pilot Testing** to determine:
  - whether the intervention’s effects can be replicated in larger samples using a control condition
  - what is the appropriate control condition & how does it behave

- **Feasibility Pilot Testing** to determine:
  - whether the intervention is feasible & acceptable
  - Numbers available for screening & recruitment
  - Estimates of yield (screening to enrollment ratio), drop-out rate, crossovers, adherence to treatment

- **Study Designs & Methods:**
  - Randomized designs
  - Can include qualitative methods to understand patient experiences, acceptability, feasibility
Limiting dietary variety in family-based treatment: 6-month pilot study (Epstein et al, 2015)

- 24 families, with a child ≥ 85th percentile BMI and aged 8 to 12 years
- Randomly assigned to 1 of 2 conditions:
  - Family-Based Treatment (FBT)
    - Traffic Light Diet (1000-1500 kcal/day, < 2 servings/day of RED foods)
    - Developed meal plans
    - ≥ 60 min/day of MVPA prescription
  - FBT+Variety
    - Family-based treatment (identical to FBT)
    - Identified two RED foods to consume during the intervention: one dinner entrée and one snack food
    - Developed meal plans that repeated dinner entrees and included leftovers from the dinner entrees and reduced variety of RED foods

- Outcomes:
  - Child percent overweight: FBT+Variety −15.4% vs. FBT − 8.9%, p = 0.017
  - Variety of RED foods consumed by family: FBT+Variety = 20.2 to 12.6 vs. FBT = 19.7 to 16.8, p = 0.01
Epstein et al, 2015
ORBIT Behavioral Intervention Development Model: Key Features

- **Begin with the “end” in mind**
  - Process is guided by “significant clinical questions” from end users – patients, providers

- **Progression** from basic to more clinical/applied stages
  - *Pushes* toward the efficacy trial

- Each phase includes “*clinically meaningful*” milestones
  - Specify *a priori* criteria for moving to next phase of the intervention development process
  - Emphasis is on achieving “clinically significant” (not just statistically significant) change in behavioral targets

- **Flexibility** in terms of:
  - Number & types of studies within phases
  - Duration of each phase
  - Movement from one phase to the next (can “skip” a phase if necessary)

- Flow is *bi-directional*
  - Allows for “failure” & return to earlier phases as needed
ORBIT & behavioral intervention development: Lessons learned

- **Reconceptualize & de-stigmatize “failure”** – it’s ok if you don’t find what you expect!

- Often a “failure” to move forward to next phase is positive – means an opportunity to refine ideas, drill down to better understand mechanism, try a different approach, revise theory, improve potency of intervention

- There is value in the “fail early” philosophy behind early-phase translation/behavioral intervention development – promising ideas that do not meet preliminary efficacy goals do not go on to more expensive Phase III trials, saving time & cost
The formation of cross-disciplinary teams is key – much is gained by involving diverse disciplines in the intervention development process & “vetting” ideas with other members of a research team, as well as with the larger network.

"Look, I know you and I have had our differences, but can we at least agree that the goldfish is pointless?"
Thanks to all my colleagues who participated in ORBIT

Questions?