

Does Acceptance and Relationship Focused Behavior Therapy Contribute to Bupropion Outcomes? A Randomized Controlled Trial of Functional Analytic Psychotherapy and Acceptance and Commitment Therapy for Smoking Cessation

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This study evaluated a treatment combining bupropion with a novel acceptance and relationship focused behavioral intervention based on the acceptance and relationship context (ARC) model. Three hundred and three smokers from a community sample were randomly assigned to bupropion, a widely used smoking cessation medication, or bupropion plus functional analytic psychotherapy (FAP) and acceptance and

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commitment therapy (ACT). Objective measures of smoking outcomes and self-report measures of acceptance and relationship processes were taken at pretreatment, posttreatment, 6-month, and 1-year follow-up. The combined treatment was significantly better than bupropion alone at 1-year follow-up with 7-day point prevalence quit rates of 31.6% in the combined condition versus 17.5% in the medication-alone condition. Acceptance and the therapeutic relationship at posttreatment statistically mediated 12-month outcomes. Bupropion outcomes were enhanced with an acceptance and relationship focused behavioral treatment.

Keywords: smoking cessation treatment; therapeutic relationship; acceptance and commitment therapy; functional analytic psychotherapy; bupropion

TOBACCO USE REMAINS THE single most preventable cause of death, contributing to over 443,000 deaths

per year in the United States and almost 5 million deaths worldwide (Centers for Disease Control and Prevention [CDCP], 2010; Schroeder, 2004). Most smokers want to quit, with 50% making a quit attempt annually (CDCP, 2004), but of the current 46 million U.S. smokers (1 of 5 adults) only 2.5% will quit successfully in any given year (Fiore et al., 2000). In spite of widely disseminated information about the adverse health effects of smoking, the rate of decline has slowed over the past 5 years (CDCP, 2010), further indicating the need to improve smoking cessation treatment.

BUPROPION AND BEHAVIOR THERAPY

Bupropion is the only nonnicotine front-line pharmacotherapy for tobacco use (Fiore et al., 2008; Killen et al., 2006). Bupropion is often prescribed without behavioral treatment, despite recommendations for adjunctive behavioral counseling (Kohlenberg, Antonuccio, Hayes, Gifford, & Piasecki, 2004). This dissemination pattern, in which combined behavioral and pharmacological treatment recommendations result in monotherapy medication use, has been documented in antidepressant treatment more broadly (Antonuccio, Danton, DeNelsky, Greenberg, & Gordon, 1999; Olfson & Marcus, 2009).

There is limited research on the efficacy of bupropion without concomitant psychosocial intervention (McCarthy et al., 2008). Most pharmacotherapy trials include counseling. For example, in a recent meta-analysis of bupropion and other smoking medications, the authors provided odds ratios of medication treatment outcomes only in combination with counseling (i.e., without identifying the effect size of medication treatment alone; Eisenberg, Fillion, Yavin, Belisle, Mottillo, Joseph, et al., 2008). While balancing counseling between active and placebo medication study arms makes it possible to evaluate significance levels, it does not lead to precise effect-size estimates for medication without counseling, a point that is easily overlooked by health professionals and may contribute to the field's propensity to pay less attention to adjunctive counseling (Antonuccio and Danton, 1999; Olfson & Marcus, 2009).

The impact of counseling on bupropion outcomes is also unclear. Of the few bupropion studies evaluating the impact of adjunctive counseling, most indicate that behavioral treatment does not improve outcomes (Hall et al., 2002). In a recent randomized placebo control trial bupropion had a modest significant effect that dissipated 1 year after treatment and counseling did not significantly increase bupropion's efficacy at any time point (McCarthy et al., 2008). Another study evaluating

the impact of telephone counseling on bupropion treatment showed no significant difference at 3-month follow-up, but at 9-month follow-up those who received counseling were significantly more likely to have quit. The authors attribute these results to a possible "sleeper effect" (Swan et al., 2003). Even when counseling does not contribute meaningfully to overall bupropion treatment outcomes, certain aspects of counseling interventions may be more or less related to outcome (McCarthy et al., 2010).

The present randomized trial tested the impact of adding a behavioral treatment composed of functional analytic psychotherapy (FAP; Kohlenberg & Tsai, 1991) and acceptance and commitment therapy (ACT; Hayes, Strosahl, & Wilson, 1999) to bupropion treatment for smoking cessation. The goal was to evaluate whether the combined treatment, designed to maximize relationship and acceptance processes, would show better outcomes than treatment with bupropion alone, and whether theoretically specified acceptance and relationship proximal outcomes would predict long-term smoking outcomes. If so, further efforts might focus on understanding and improving the elements of counseling that contribute to positive effects (Gifford, 2008; Kazdin, 2001; Morgenstern & McKay, 2007).

THE ACCEPTANCE AND RELATIONSHIP CONTEXT MODEL

The FAP and ACT smoking treatment was based on the acceptance and relationship context model (ARC), a functional model of treatment process (Gifford, Ritsher, McKellar, & Moos, 2006). ARC specifies that supportive, engaging treatment relationships and acceptance of internal states facilitate constructive behavior change (Carrico, Gifford, & Moos, 2007; Gifford et al., 2006). A number of studies have shown that treatment outcomes may be improved by helping patients learn to accept internal states rather than engaging in maladaptive avoidance (Hayes, Luoma, Bond, Masuda, & Lillis, 2006). Acceptance appears to play a particularly important role in recovery from addiction. In a prospective longitudinal study of 3,500 patients in substance abuse treatment, the ARC model accounted for a large proportion of the variance in substance use outcomes at 2-year follow-up (41%; Gifford et al., 2006). Another study identified that acceptance contributes to important recovery behaviors such as 12-step involvement after treatment (Carrico et al., 2007).

Smoking offers short-term relief from negative affect and other negatively valenced states such as cravings or urges to smoke, and negatively

reinforced avoidance of these states is thought to play an important role in smoking maintenance (Baker, Piper, McCarthy, Majeskie, Fiore, 2004; Brown, Lejuez, Kahler, Strong, & Zvolensky, 2005). In order to quit, smokers must learn to accept previously avoided experiences such as nicotine withdrawal symptoms. Smokers must also learn to tolerate the urges or cravings elicited by cues associated with smoking. Powerful behavioral histories condition smoking cues that become ubiquitous in the life of a chronic smoker (Schultz, 1998). Nicotine neurochemically enhances the development of conditioned relationships (Bevins & Palmatier, 2004; Chiamulera, 2005), and research indicates that such conditioning cannot be completely eliminated (Conklin & Tiffany, 2002). This is particularly problematic because smoking cues include internal states such as negative affect that are impossible to eliminate.

Smoking cessation medications do not fundamentally resolve this problem. Bupropion is an atypical antidepressant thought to exert effects by changing dopaminergic and adrenergic tone in the mesolimbic system and striatum (among other mechanisms). Bupropion reduces but does not eliminate negative affect, withdrawal symptoms, and cravings (Durcan et al., 2002; Fryer & Lucas, 1999; Shiffman et al., 2000). Thus, even smokers treated with bupropion must learn to refrain from avoiding negative states by smoking: they must learn to accept or tolerate precisely those states that have previously led them to smoke.

The 2000 clinical practice guidelines identified the importance of helping smokers obtain social support (Fiore et al., 2000). Additional research led the 2008 panel to reinforce the importance of social support as part of the therapeutic relationship (Fiore et al., 2008). From an ARC perspective, constructive relationships help smokers undergo the difficult work of noticing and accepting their internal states rather than automatically avoiding these experiences (e.g., "I can acknowledge and accept this feeling instead of smoking to escape feeling bad"). Constructive therapeutic relationships also model and shape the acquisition of approach-based skills (e.g., "I can call a friend when I feel sad"), and facilitate contact with nonsmoking sources of reinforcement within session and through constructive behavioral activation (e.g., satisfying and supportive interpersonal interactions; Gifford et al., 2004; Grawe, 2007; Kohlenberg & Tsai, 1991). Previous studies using the ARC model indicate that constructive treatment relationships lead to improved acceptance, which leads in turn to improvements in long-term outcomes (Carrico et al., 2007; Gifford et al., 2006).

Interestingly, recent neurobiological models indicate that acceptance and supportive relationships may be related at the neuronal level, with increases in socially rewarding interactions contributing to increases in distress tolerance (Trafton & Gifford, 2010). Socially reinforcing interactions may reduce short-term reactivity to cues through alterations in dopaminergic circuits in the nucleus accumbens and other neurobiological processes (Gifford, 2007; Trafton & Gifford, 2008).

ACT AND FAP

Acceptance is defined as the ability to experience painful thoughts, feelings, memories, or other internal stimuli without automatically avoiding them, (i.e., to be present with one's experience in order to make constructive behavioral choices (Gifford et al., 2006). Several cognitive behavioral treatments emphasizing acceptance have been developed in recent years, including ACT, dialectical behavior therapy (DBT; Linehan, 1993), and mindfulness-based cognitive therapy (MBCT; Segal, Williams, & Teasdale, 2002). These treatments explicitly integrate mindfulness practices that focus on helping clients increase acceptance of present states. ACT applies a number of treatment components toward accomplishing this goal, including training in the active embrace of emotion, learning to look mindfully and dispassionately at the unfolding of thought rather than merely looking at the world structured by thought, increasing awareness of the present moment, encouraging contact with a transcendent sense of self, clarifying and engaging with values, and building patterns of committed action even in the presence of difficult emotions. Together these components are thought to promote acceptance and psychological flexibility (Gifford, 2001), the ability to persist in or change behavior in the service of chosen values rather than in the service of short-term relief (Gregg, Callaghan, Hayes, & Glenn-Lawson, 2007). Research indicates that ACT reduces the impact of negative thoughts and feelings on behavior by reducing avoidance and inflexibility, allowing clients to accept internal states and thereby engage in more adaptive, flexible, values-based action (Gifford & Lillis, 2009; Hayes et al., 2006).

ACT has been shown to be helpful with substance use disorders (Hayes, Strosahl, et al., 2004; Hayes, Wilson, et al., 2004; Twohig, Shoenberger, & Hayes, 2007) and has compared favorably to nicotine replacement in a small ($N=76$) smoking cessation treatment randomized trial (Gifford et al., 2004). In that study, objectively monitored cessation rates at 1-year follow-up were superior for the ACT condition (35% vs. 11%; Cohen's $d=.57$). This outcome

was mediated by the degree to which participants responded in an accepting and flexible way to smoking-related feelings, thoughts, urges, cravings, and sensations as measured by the Avoidance and Inflexibility Scale (AIS; Gifford, 2001; Gifford et al.). Another small trial found ACT more effective than traditional CBT for Spanish smokers (Hernández-López, Luciano, Bricker, Roales-Nieto, & Montesinos, 2009). ACT methods have also shown promise in the treatment of highly distress-intolerant smokers (Brown et al., 2008).

In order to maximize interpersonal opportunities for developing acceptance, ACT was implemented along with FAP, a behavior analytic therapy designed to maximize the potency of interpersonal processes within treatment. FAP therapists are trained to develop intimate and rewarding therapeutic relationships with their clients and then to apply the natural, genuine social reinforcement between the client and therapist contingently in order to enhance functional client repertoires in session (Tsai, Kohlenberg & Kanter, 2010). Research suggests that FAP training can improve therapists' use of contingent interpersonal feedback within the treatment session, and that client repertoires reinforced by FAP therapists generalize beyond the treatment setting (Callaghan, Summers, & Weidman, 2003; Kohlenberg, Kanter, Bolling, Parker, & Tsai, 2002).

In the present study, FAP was used to create increased attention to the therapeutic relationship in session and to reduce avoidant responding by contingently reinforcing acceptance of previously avoided material (e.g., accepting the discomfort of revealing difficult personal experiences with the group members, or tolerating discomfort in the interaction with the therapist; Cordova & Kohlenberg, 1994). ACT and FAP are particularly easy to use together because they share a common behavior analytic theoretical base (Kohlenberg, Hayes, & Tsai, 1993), and case reports successfully integrating ACT and FAP have been reported in the literature (Paul, Marx, & Orsillo, 1999).

Method

PARTICIPANTS

Adult nicotine-dependent smokers were recruited from the community through television coverage (a local news channel), newspaper and radio advertisements, referrals from physicians and agencies, announcements at community groups such as churches and Indian Health Service staff meetings, and flyers. Study psychiatrists conducted semistructured screening interviews informed by screening measures (Beck Anxiety Inventory [BAI], Beck Depression Inventory [BDI], Fagerstrom Test for Nicotine Dependence [FTND], and Cut-Down,

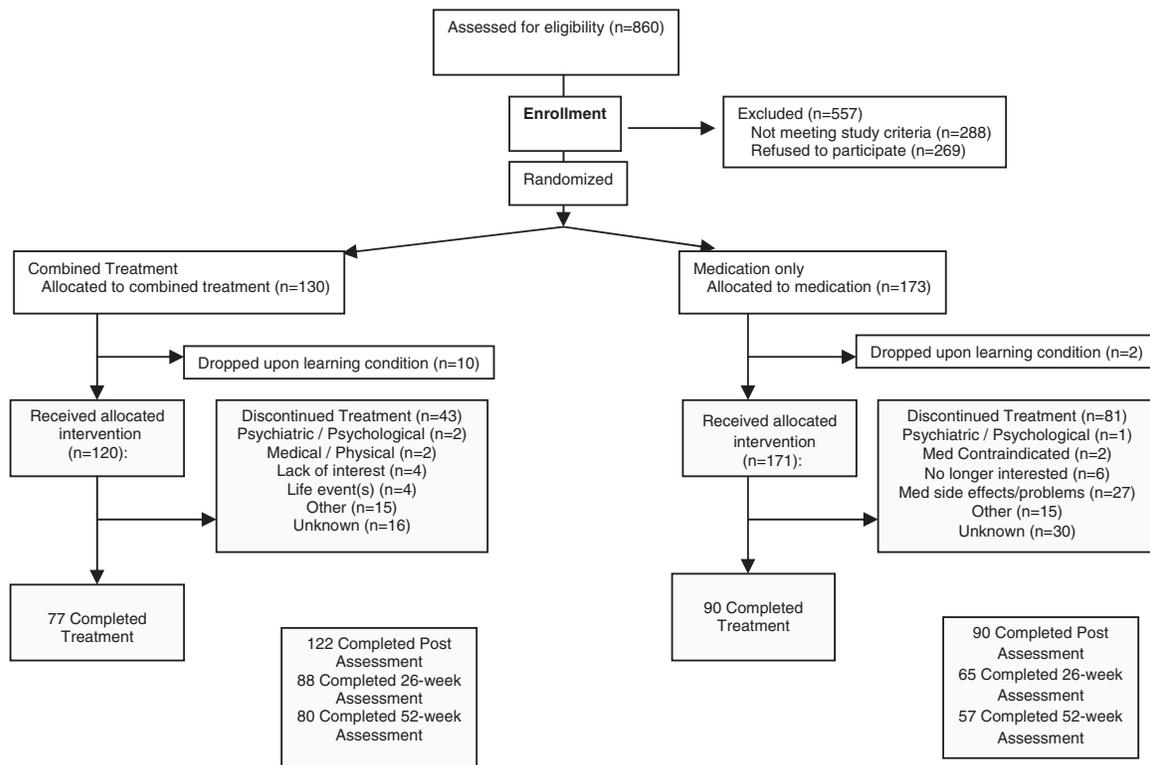


FIGURE 1 Progression through study from initial telephone contact.

Table 1
Inclusion and Exclusion Criteria

Exclusion Criteria	Inclusion Criteria
Current problem drinking (CAGE score of 2 or more) or diagnosis of alcohol or drug dependence within the last year (excluding nicotine)	Self-identification as a nicotine dependent smoker, smoking 15 cigarettes or more per day for at least twelve months with FTND scores of 5 or more
A history or current diagnosis of anorexia nervosa or bulimia	Willingness to be randomly assigned to treatment
Current use of tobacco products other than cigarettes	Willingness to continue with the project for the full 10-week treatment period
Current use of nicotine-replacement therapies, fluoxetine, clonidine, bupropion, or doxepin	Willingness not to seek other treatment for smoking during the 10-week active treatment period
Active affective disorders, including Major Depressive Disorder, Bipolar Disorder, or Anxiety disorders	At least one quit attempt in the past two years that resulted in abstaining from nicotine for at least 24 hours
Unstable medical or psychiatric condition	
Under eighteen years of age	
A personal or family history of seizures	
A personal history of head trauma	
Pregnancy or lactation	
Non-English speaking	
Only one participant per household	

Annoyed, Guilt, Eye-Opener [CAGE], (see Fig. 1; see Table 1 for inclusion and exclusion criteria). After informed consent and intake assessment, the research director used a random numbers generator (<http://www.randomizer.org>) to randomly assign participants to condition and the study coordinator was notified about assignment after participants were accepted into the study. Participants were notified of assignment by the study coordinator. Of the 303 participants, women made up 58.7% of the final sample and ethnic minorities comprised 11%, with the largest minority groups being Native American (4.2%) and African American (2.6%). Caucasian participants composed 86.8% of the sample and 2.3% did not report their ethnicity/race. The participants' ages ranged from 18 to 75 years old, with a mean of 45.99 years ($SD=12.5$). Forty-two percent reported a family income below \$30,000. Seventy-one percent reported completing at least some post-high school education, 21.9% reported receiving a high school diploma, and 4.8% reported only completing some high school.

Participants reported smoking an average of 24 cigarettes per day ($SD=9.04$), with a history of 2.15 quit attempts that lasted at least 1 day over the past 2 years ($M=2.15$, $SD=3.64$). The length of participants' longest previous quit attempts varied widely, with a median of 21 days ($M=192.51$, $SD=560.17$, range=1–4,745). Thirty-eight percent of participants reported no previous smoking cessation treatment.

MEASURES

The BAI, BDI, FTND, and CAGE screening measures were conducted at intake, and the Client Satisfaction Questionnaire (CSQ) at posttreatment. All other measures were taken at baseline, posttreatment, 6-month, and 12-month follow-up.

Screening Measures

Beck Anxiety Inventory (BAI; $\alpha=.82$; Beck, Epstein, Brown, & Steer, 1988). The BAI is a well-established measure of anxiety consisting of 21 items on a 4-point scale, each describing a common symptom of anxiety. We employed a cutoff screening score of 20 (Beck, 1987).

Beck Depression Inventory–II (BDI-II; $\alpha=.82$; Beck & Steer, 1984). The BDI-II assesses the intensity of depression in clinical and nonclinical samples with 21 items assessing severity of depression symptoms, with a cut-off screening score of 20 (Beck, 1990).

Cut-Down, Annoyed, Guilt, Eye-Opener (CAGE; $\alpha=.35$; Shields & Caruso, 2004). The CAGE is a brief, 4-item questionnaire that assesses the need to reduce drinking, with 2 or more “yes” responses considered indicative of problems with drinking.

Fagerstrom Test for Nicotine Dependence (FTND; $\alpha=.42$; Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). The FTND includes 6 items with a total score that ranges from 1 to 10. A score of 6 or above indicates high dependence.

Brief Stages of Change (SOC; $\alpha=.32$; Prochaska, DiClemente, & Norcross, 1992). The brief SOC is a widely used 5-item measure of motivational stages regarding readiness to quit smoking, which was used to evaluate whether randomization resulted in similarly motivated groups at baseline.

Outcome Measures

Smoking Outcomes: Seven-day point prevalence confirmed with expired carbon monoxide (CO). The primary outcome measure was verified smoking abstinence. Participant reports of 7-day point prevalence abstinence were considered verified if breath samples indicated ten parts per million or less carbon monoxide (CO) using the breath-holding procedure

described by Irving, Clark, Crombie, and Smith (1988).

Client Satisfaction Questionnaire-3 (CSQ-3; $\alpha=.86$; Nguyen, Attkisson, & Stegner, 1983). The CSQ-3 measures client satisfaction with treatment services. The 3 items are rated on a 4-point Likert scale, with higher scores indicating greater client satisfaction.

Process Measures

Shiffman Tobacco Withdrawal Scale (STWS; $\alpha=.69$; Shiffman & Jarvik, 1976). The STWS measures symptoms associated with cigarette withdrawal, with 25 items averaged for a total score. The scale has been validated in the study of withdrawal and is widely used (Patten & Martin, 1996).

Profile of Mood States (POMS; $\alpha=.91$; McNair, Lorr, & Droppleman, 1971). The POMS is a measure of mood yielding 6 subscale scores (depression-dejection, tension-anxiety, anger-irritability, confusion, fatigue, and vigor) and a total mood disturbance score. According to Patten and Martin (1996), the POMS “should be included in any comparison of the self-report measures of tobacco withdrawal” (p. 105).

Avoidance and Inflexibility Scale (AIS; $\alpha=.96$; Gifford, 2001; Gifford et al., 2004). The AIS was designed to measure avoidant and inflexible responding to internal stimuli, including thoughts, feelings, and bodily sensations. It consists of 13 Likert-style items, scored on a scale of 1 to 5, evaluating participants’ responses to their cognitions, affect, or physiological sensations. For example, “How much are you struggling to control physiological sensations linked to smoking?” and “To what degree do you accept feelings associated with smoking?” Lower scores indicate a more accepting and flexible response to internal states associated with smoking. Higher scores indicate a more avoidant and inflexible response to internal states associated with smoking (e.g., feelings about smoking automatically lead to smoking, and refraining from smoking requires avoiding these feelings).

Acceptance and Action Questionnaire (AAQ; $\alpha=.59$; Hayes, Strosahl, et al., 2004; Hayes, Wilson, et al., 2004). The AAQ is a 9-item questionnaire that measures general levels of experiential avoidance. Lower scores reflect greater willingness to experience difficult thoughts and feelings. Items include, “I often catch myself daydreaming about things I've done and what I would do differently next time” and “I rarely worry about getting my anxieties, worries, and feelings under control” (reverse scored).

Working Alliance Inventory (WAI; Horvath & Greenberg, 1989; $\alpha=.97$). The WAI is a 12-item measure of the therapeutic relationship widely used as a general measure of “the extent to which a client and therapist work collaboratively and purposefully and connect emotionally” and is considered a global measure of working alliance (Hanson, Curry, & Bandalos, 2002, pp. 659–660). Higher scores indicate better relationships.

TREATMENT

Bupropion Regimen

Slow release (SR) bupropion was provided to all participants in both conditions free of charge, prescribed according to the standard dosing regimen of 150 mg once per day for the first 3 days followed by 150 mg twice per day (separated by 8 hours or more). These medications were not provided by pharmaceutical company research funding. Participants were treated by a board certified psychiatrist with extensive training in the medical management of smoking cessation and a psychiatry resident under her supervision. The psychiatrists monitored adverse reactions to the medication and vital signs and were on 24-hour call throughout treatment.

All participants in both conditions were assigned a quit date 10 days after initiating bupropion in accordance with manufacturer recommendations. All participants attended a 1-hour medication instruction group presenting the rationale for bupropion and were given a medical release form, staff contact information, and detailed instructions. Participants received medication refills and checks on medication usage and possible adverse events one to two times during treatment. Timeline follow back (TLFB) interviews were conducted during each visit to determine medication adherence. If the participant had more than 3 nonconsecutive nonadherent days (i.e., taking one or fewer pills per day) or more than 2 consecutive nonadherent days they were rated nonadherent for that week. Prescriptions were terminated after the 10-week treatment period.

Combined Treatment

Behavioral and bupropion treatment began and ended simultaneously. In addition to the bupropion regimen procedure, counseling participants attended one group and one individual session per week for 10 weeks, with treatment delivered according to individual and group treatment manuals. Therapy was provided by one master's-level substance abuse therapist and three master's-level clinical psychology doctoral students with previous training in ACT and/or FAP (manuals are available from www.contextualpsychology.org). Participants were asked to record their smoking for the first 10 days of

treatment prior to their quit date but were not advised to change their smoking during this time in accordance with bupropion recommendations.

The treatment protocol retained the ACT elements in Gifford et al. (2004), using FAP principles to help enhance the relationship, inform case conceptualization, and enhance contingent shaping of acceptance repertoires throughout treatment. FAP uses the therapeutic relationship to elicit and modify clinically relevant functional classes of behavior within the treatment session. The therapeutic relationship is both a context in which new repertoires may emerge and a source of reinforcement.

Therapists used the therapeutic relationship to elicit and reinforce positive behavioral steps taken by the client. This might include focusing the client on difficult feelings in the present by asking such questions as, "How do you feel about being in treatment today?" The discomfort of discussing negative feelings would be linked to the discomfort of refraining from smoking, providing a direct experience of responding in new and different ways (coming to treatment while experiencing resistance, expressing awkward feelings about treatment to the therapist) while experiencing discomfort.

FAP ideographically determines which repertoires to reinforce according to the case conceptualization. Because of its purely functional nature, the FAP intervention elements occurred throughout the more structured ACT interventions. Supervision provided the primary mode of support for this functional intervention. All individual and group sessions were videotaped and therapists received weekly group supervision with videotape review. Therapists also received individual supervision as judged appropriate by the supervision team.

Individual and group treatment sessions were designed to be mutually supportive. Issues raised during group might be followed by further individual work on the same topic. Some elements of traditional cognitive behavioral approaches to smoking were retained (e.g., a discussion of external triggers) but were addressed within an acceptance-based approach (e.g., "change what you can and accept what you cannot change"). Mindfulness exercises were used in most group sessions in order to practice awareness of internal states from a nonreactive perspective. Both group and individual sessions provided opportunities to engage in exposure to the thoughts and feelings that might ordinarily lead to smoking, while learning to respond to those cues in a mindful, accepting manner. Beginning initially with mindful smoking exercises during breaks, in which awareness of the range of sensations prior to and during smoking could be examined, group sessions proceeded to mindful breaks without smoking, and

ultimately to handling cigarettes, lighters, and other smoking-related items while practicing acceptance and mindfulness skills. Group cohesiveness was promoted by interpersonal exercises in which members shared feelings and experiences throughout treatment. For example, participants were encouraged to approach treatment termination as an opportunity to practice acceptance and mindfulness skills with their treatment providers and fellow group members regarding the end of the supportive relationships within the treatment setting. Individual sessions were viewed as opportunities to practice the skills learned in group, using interpersonal opportunities that arose during these sessions to shape in vivo development of acceptance skills.

Treatment Integrity

The ACT Tape Rating Scale (Gifford & Hayes, 1998), an ACT treatment integrity subscale based on the Project MATCH Tape Rating Scale (Carroll et al., 1998), was expanded to develop the Functional Acceptance and Commitment Therapy Scale (FACTS; Pierson, Bunting, Smith, Gifford, & Hayes, 2004) to assess treatment integrity in the present study. The FACTS is composed of 15 items, with 14 items referring to specific treatment components (9 items measure treatment-consistent components such as "Explore clients' efforts to control thoughts and feelings," "Comment on clients' in-session behavior"; 5 items measure treatment-inconsistent components such as "Substituting positive thoughts"; and 1 item measures global competence; Shaw, 1984). Each item is rated from one to five ranging from "not present at all" to "demonstrated often and thoroughly during the session."

Three raters scored complete individual and group session tapes. For both the individual and group sessions, the first and last sessions for each participant were excluded and 25% of the remaining available tapes were randomly selected, 85 individual sessions and 18 group sessions. The raters were three graduate students with at least 1 year of graduate training and supervision in ACT and/or FAP. Raters received approximately 10 hours of training and reliability was evaluated using intra-class correlation coefficients (ICC, model 2, 1; Shrout & Fleiss, 1979).

Results

POWER

Based on previous bupropion studies (Hurt et al., 1994), 80% power at an alpha level of .05 (two tailed) to detect a difference of 20% versus 35% in abstinence levels between the treatment and comparison groups at posttreatment (OR=2.13) required a sample size of 144/cell, which was the cell size attempted for this study.

EQUIVALENCE OF COMPARISON GROUPS

Two-tailed *t* tests for continuous variables and chi-square for categorical variables revealed no significant differences between conditions in baseline demographic variables (age, gender, income, education, ethnicity, relationship status), smoking variables (number of cigarettes smoked, length of time smoked, FTND scores, previous treatment for smoking, number of previous 24-hour quit attempts), motivation to quit smoking (see Table 2), or process variables (see Table 3).

ATTRITION

Of the 303 participants who entered treatment, 212 (70%) completed the posttreatment assessments and 229 (75.5%) completed at least one follow-up assessment. Ten participants in the combined condition and two in the medication-alone condition were randomized to condition and did not start treatment. Participant attendance at behavioral treatment sessions was recorded by clinic administrative personnel at the time of appointments and

verified by clinical chart review. Medication use for participants in both conditions was verified during prescription refill appointments using TLFB.

Using the intent-to-treat sample, there were no significant differences in treatment completion rates between the combined (77/130; 59%) and medication-only conditions (90/173; 52%). There was a significant difference between conditions when including only those who started treatment (combined condition 77/120, 64%; medication alone 90/171, 52%, $p < .05$). There was no significant difference between groups in treatment adherence. The combined treatment group used on average 84 ($SD = 42$) pills and the medication-only group used on average 89 ($SD = 46$), which was not significantly different ($t = -.76$, $p = .45$) and which constitutes an average of 6 weeks of medication use. Participants in both conditions were considered completers if they completed at least 5 verified weeks of treatment. Attrition rates for smoking treatment studies range from 10% to 50% (Curtin, Brown, & Sales, 2000), which places the rates for the present study in the

Table 2
Tests for Preexisting Differences Between Groups

Pearson's χ^2 tests for preexisting difference between groups

Variable	χ^2	<i>df</i>	<i>N</i>	<i>p</i>
Gender	0.89	1	303	.21
Ethnicity	7.73	6	303	.26
Education	2.69	5	303	.75
Family Income	3.48	7	298	.84
Personal Income	11.39	7	301	.12
Marital Status	6.00	6	303	.42
Past Treatment	0.02	1	301	.89

T-tests for preexisting differences between groups

Variable	<i>M</i>	<i>SD</i>	<i>t</i>	<i>df</i>	<i>p</i>
Age					
Combined	45.75	12.84	-.28	300	.78
Medication Only	46.16	12.28			
Quit Attempts Past 2 Years					
Combined	1.92	2.03	-.93	292	.35
Medication Only	2.32	4.43			
Number of cigarettes per day					
Combined	24.01	8.64	-.21	301	.84
Medication Only	24.23	9.35			
Nicotine dependence					
Combined	5.22	1.69	-.51	298	.61
Medication Only	5.32	1.66			
Months smoking					
Combined	335.58	161.99	.13	298	.90
Medication Only	333.15	157.54			
Motivation ^a					
Combined	2.70	.541	-.569	301	.57
Medication Only	2.73	.546			

^a Stage of Change.

Table 3
Means and Standard Deviations for Mediator Variables

	Combined		Medication Only		Group Difference ^a
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	
Intake AIS Score	49.3	7.9	48.9	7.8	
Post AIS Score	30.4	14.5	40.0	13.9	$F(1,208)=25.77^{**}$
Intake AAQ Score	28.3	5.7	30.4	6.3	
Post AAQ Score	28.0	6.4	29.1	6.9	$F(1,208)=.03$
Intake STWQ Score	104.0	9.8	103.0	9.8	
Post STWQ Score	114.6	13.0	110.5	10.7	$F(1,204)=5.56^*$
Intake POMS	-6.4	18.2	-3.0	18.6	
Post POMS	1.7	31.2	4.3	25.0	$F(1,187)=.39$
Post WAI Score	68.8	12.6	52.2	9.0	$t(195)=10.72^{**}$

Note. AIS = Avoidance and Inflexibility Scale, AAQ = Acceptance and Action Questionnaire, STWQ = Shiffman Tobacco Withdrawal Questionnaire, POMS-TMD = Profile of Mood States – Total Mood Disturbance, WAI = Working Alliance Inv.

^a group differences were as assessed by an analysis of covariance with the pre-score as a covariate or in the case of the WAI, a *t*-test.

* $p \leq .05$; ** $p \leq .01$.

high normal range, 41% in combined and 48% in medication-alone conditions. Those participants who dropped out of the study were not significantly different from those who completed the study on any of the baseline measures, demographics, or smoking variables. Treatment was not associated with dropping out and there were no significant differences in dropout between conditions at posttreatment, $\chi^2(4, N=212)=.219, p=.64$, 6-month, $\chi^2(4, N=153)=.103, p=.75$, or 12-month follow-up, $\chi^2(4, N=137)=.000, p=.99$.

TREATMENT ACCEPTABILITY

One purpose of the present study was to see if a relationship and acceptance based treatment would be well accepted in combination with medication. Those in the combined treatment condition showed a significantly higher level of treatment satisfaction (CSQ-3) at the posttreatment assessment compared to those in the medication-alone condition (combined: $M=10.47, SD=2.02$; medication alone: $M=8.68, SD=2.26; t=5.73, p<0.0001$, Cohen's $d=.84$). These differences persisted at 6 months (combined: $M=10.08, SD=2.03$; bupropion alone: $M=8.40, SD=2.51; t=4.89, p<0.0001$, Cohen's $d=.72$), and 1 year after treatment (combined: $M=10.10, SD=2.15$; bupropion alone: $M=8.44, SD=2.38; t=4.43, p<0.0001$, Cohen's $d=.73$).

TREATMENT INTEGRITY

Intraclass correlation coefficients for videotape ratings ranged from .82 to .99, with a mean rating of .93 and an *SD* of .036 (ICC, model 2, 1; Shrout & Fleiss, 1979) and reliability for the group tapes was similar (.88 – .96, $M=.93, SD=.02$). All of the rated tapes met the previously set criterion for adherence to treatment consistent components, which was a scale mean greater than or equal to 2

(Gifford et al., 2004). This value reflected the fact that topics addressed by some items were not scheduled to be covered in given sessions (e.g., an adherent therapist could address one topic extensively and others very little during a particular session). On the global competence item the five study therapists averaged above 4 (on a 5-point scale) for both individual and group sessions (for individual sessions, $M=4.29, SD=.78$, range=2 to 5; for group sessions, $M=4.78, SD=.43$, range=4 to 5). Global competence was significantly correlated with total adherence as measured by the average score on the 9 treatment-consistent items ($r_s=0.49, p<0.001$) and not with the average for the 5 treatment-inconsistent items ($r_s=-0.09, p=0.40$). None of the group sessions contained any treatment-inconsistent components and only 2% of the individual sessions contained any treatment-inconsistent therapist behaviors (i.e., a score above 1 on any of the inconsistent items). The proscribed items in these sessions did not differ significantly from zero (one item was 100% zero, in the other 98% of cases were zero, and 2% had a level of changing cognitions that did not differ significantly from zero, $t=1.42(84), p=.16$). All treatment-consistent items differed significantly from zero (t ranging from 11.55 – 26.24 [84], $p=.000$ for all items). Thus, study therapists appeared to deliver the treatment as intended.

SMOKING OUTCOMES

Obtained Data

Using data posttreatment (10 weeks post quit date), 7-day point prevalence quit status differed significantly between conditions, $\chi^2(1, N=212)=10.85, p<.001$, Cohen's $d=.46$, Cramer's $V=.23$, with 50.0% quit in the combined group compared with 27.9% quit in the bupropion alone group. The

interim 6-month assessment was not significantly different, with 26.2% quit in the combined group versus 18.2% quit in the medication alone group, $\chi^2(1, N=153)=1.41, p=.162$. However, at 1-year follow-up, differences in 7-day point prevalence quit status were again statistically significant, with 31.6% quit in the combined treatment versus 17.5% in the medication-alone condition, $\chi^2(1, N=137)=3.69, p=.044$, Cohen's $d=.33$, Cramer's $V=.16$. Focusing only on participants with data at all time points, 36.6% of the combined condition participants were continuously abstinent (defined as 7-day point prevalence quit status at all time points) compared to 17.5% of the medication-only participants, a statistically significant difference, $U(98)=946, z=2.12, p=.034$. Fig. 2 shows the percentage of each group abstinent at post, 6 months, and 1 year after treatment.

Intent to Treat

The data were examined in several ways to ensure that missing data could not account for the outcomes seen in the obtained data. Out of the 303 participants, 229 (75.6%) completed at least one follow-up assessment. 502 observations (73.1%) were available of the 687 possible observations for these participants (229 participants at 3 time points).

Since none of the measures of interest were significantly related to attrition (see previous section on dropout), GEE was initially used to calculate differences in quit status across groups and time. GEE develops its estimates from using all available data and incorporates the effects of time (Hall et al., 2001). Results showed the same pattern as with obtained data. Averaged over all time points posttreatment, the combined treatment was significantly more effective in reducing smoking ($\beta=0.789, p<0.001$), with an odds ratio of 2.20 more likely to quit. Although GEE handles

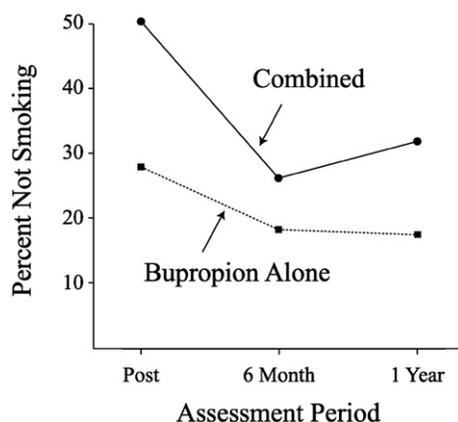


FIGURE 2 Smoking outcomes by treatment condition.

missing data relatively well (Hall et al., 2001), two additional intent-to-treat analyses were conducted given study attrition. The first additional outcome analysis was conducted using R software (www.r-project.org) to conduct multiple imputations of missing data. The GEE results remained the same (treatment group differences $\beta=0.764, p<0.001, OR=2.15$). Finally, because reasons for attrition from follow-up were not clear, a mixed effects nominal logistic regression was conducted using MIXNO software (<http://tigger.uic.edu/~hedeker/mix.html>). Mixed models can adjust for missingness accounted for by study variables (Hedeker & Gibbons, 2006), which is a more conservative assumption regarding missing data than GEE. Once again, treatment group differences were significant ($p<.002$).

PROXIMAL OUTCOMES

Five process variables measured posttreatment were examined for their ability to meet statistical mediation requirements for combined treatment outcomes at 1-year follow-up, including possible psychological mechanisms of action for bupropion, withdrawal symptoms (STWS) and negative affect (POMS), and processes specified by the ARC model, the therapeutic relationship (WAI), avoidance and inflexibility (AIS), and a general measure of experiential acceptance (AAQ).

Mediation was initially calculated using Baron and Kenny's (1986) causal steps model, which requires a statistically significant a path (treatment to mediator), b path (mediator to outcome controlling for treatment), and c path (treatment to outcome), as well as a reduction in the magnitude of the c path when adjusted for the mediator (the c' path). As is shown in Tables 4 and 5, the mediators that met Baron and Kenny's basic requirements were withdrawal symptoms, smoking-related acceptance as measured by the AIS, and the therapeutic relationship (Table 4). However, withdrawal symptoms did not retain significance as a mediator in the final model (see Table 5).

For those variables that showed mediation in the causal steps model, the statistical significance of the indirect effect ($c - c'$) was formally assessed by examining the cross-product of the ab coefficients (MacKinnon & Dwyer, 1993). This approach is widely recognized as the best all-around method to test mediation (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002) because it directly examines the significance of the difference between the direct and indirect, or mediated, effect (Sobel, 1982). Mediation was first examined using Sobel's (1982) error term for the cross-product, which can be used with dichotomous dependent variables (MacKinnon

Table 4
Hypothesized Mediators at Posttreatment and 12-Month Outcomes by Condition ^a

Hypothesized mediators	The relationship between hypothesized mediators and treatment condition ^b			12-month outcome ^c				
	<i>B</i>	<i>SE</i>	<i>P</i>	<i>B</i>	<i>SE</i>	<i>p</i>	OR	95% CI
Post								
AIS	9.881	1.946	<.001	-0.068	0.017	<.001	0.934	0.903–0.965
AAQ	0.135	0.738	.182	-0.026	0.036	.471	0.974	0.907–1.046
STWQ	-3.617	1.534	.019	0.044	0.020	.031	1.045	1.004–1.088
POMS-TMD	-2.312	3.705	.533	-0.012	0.011	.273	0.988	0.967–1.009
WAI	-16.559	1.544	<.001	0.041	0.015	.006	1.042	1.012–1.073

^a Controlling for the hypothesized mediators baseline scores for all but the WAI which is measured at post only. AIS = Avoidance and Inflexibility Scale, AAQ = Acceptance and Action Questionnaire, STWQ = Shiffman Tobacco Withdrawal Questionnaire, POMS-TMD = Profile of Mood States – Total Mood Disturbance, WAI = Working Alliance Inventory.

^b Results of the regression of the hypothesized mediator (dependent variable) to condition (independent variable), direction of effect = combined condition > medication alone.

^c Results of the regression of outcome (dependent variable) to the hypothesized mediator (independent variable).

& Dwyer, 1993). Both smoking-related acceptance and the therapeutic relationship were shown to be significant mediators, with the indirect effect accounting for 60% and 89%, respectively, of the total effect of condition on outcome (note, however, that these values should be interpreted with caution as they can be unstable in studies with fewer than 500 participants; MacKinnon, Fairchild, & Fritz, 2007). When smoking status was regressed on treatment condition with both mediators in the model, only acceptance-based responding remained significant (AIS $B = -.063$, $SE = .018$, $p = .001$; WAI $B = .036$, $SE = .021$, $p = .078$).

A final nonparametric mediational analysis was conducted since normal theory tests of cross-products of the coefficients assume a normal distribution, which may be incorrect (Preacher & Hayes, 2004). One way to solve the problem is through bootstrapping (Preacher & Hayes, 2004, 2008), in which k samples of the original size are taken from the obtained data (with replacement after each specific number is selected), and mediational effects are calculated in each sample. In the present set of analyses, parameter estimates were based on 3,000 bootstrap samples. The point

estimate of the indirect cross-product is the mean for these samples; the bias corrected and accelerated 95% confidence intervals are similar to the 2.5 and 97.5 percentile scores of the obtained distribution over the samples, but with z -score based corrections for bias due to the underlying distribution (Preacher & Hayes, 2004, 2008). If the confidence intervals do not contain zero, the point estimate is significant at the level indicated. The nonparametric test of mediation indicated that posttreatment levels of smoking-related acceptance and the therapeutic relationship both individually mediated 1-year follow-up smoking outcomes ($p < .05$; see Table 6). Confirming the earlier regression analysis, when a multiple mediator model was tested that included both process variables, the overall model was significant, but only acceptance remained individually significant. Although an interaction between acceptance and the therapeutic relationship is possible, this study is underpowered to evaluate whether such an interaction occurred (Hsieh, 1989). However, in the present study the therapeutic relationship and acceptance were moderately correlated after treatment ($r = -.32$, $p < .001$), with higher scores on acceptance (lower

Table 5
Relations Between Condition and 12-Month Outcome Controlling for the Hypothesized Mediators (Controlling for the Hypothesized Mediators Baseline Scores for All but the WAI)

Hypothesized mediators	<i>B</i>	<i>SE</i>	<i>p</i>	OR	95% CI	Sobel's Test	<i>p</i>	% of total effect
Post								
AIS	-0.300	0.443	.498	0.741	0.311–1.766	-3.142	<.001	69.133
AAQ	-0.728	0.406	.073	0.483	0.218–1.070	-0.177	.859	
STWQ	-0.589	0.419	.160	0.555	0.244–1.261	-1.609	.108	
POMS-TMD	-0.525	0.438	.231	0.592	0.251–1.397	0.542	.588	
WAI	0.201	0.557	.718	1.223	0.411–3.643	-2.649	<.001	77.157

AIS scores) associated with stronger ratings of the therapeutic relationship (higher WAI scores).

Discussion

The present study evaluated a novel theoretically based combined behavioral and pharmacological treatment in order to determine whether behavioral treatment could improve bupropion outcomes. Identifying the contribution of counseling to bupropion treatment is important given the paucity of studies identifying additive effects. According to a recent Cochrane review (Hughes et al., 2010), "There was no evidence from any [studies] that the efficacy of bupropion differed between lower and higher levels of behavioural support ... or by type of counselling approach used" (p. 10). In the present study results for participants in the FAP and ACT condition were significantly better overall, with effects persisting 1 year after treatment. These results were not due to unusually poor results in the bupropion-only condition. Hughes et al. found the weighted average for bupropion quit rates was 17% (2010, p.8). Using this metric, the quit rate for bupropion alone in the present study (17.5%) was within the reported literature.

An additional aim of the study was to identify whether treatment appeared to influence outcomes according to the processes specified by the theoretical model. The rationale for the combined treatment assumed that bupropion would not eliminate negative affect, withdrawal symptoms, or other internal stimuli that occasion smoking, which was indeed the case (see Table 3). Accordingly, the combined treatment aimed to attenuate the impact of internal cues on smoking using in vivo social reinforcement, interpersonal focus, and ACT interventions to help smokers learn to accept and respond adaptively to internal states.

The analysis of theoretically specified proximal outcomes provides preliminary support for the relationship and acceptance components of the

ARC model in smoking cessation. Participants in the combined condition reported stronger interpersonal relationships with their treatment providers, and these relationships statistically mediated the effect of the combined treatment on smoking status. The therapeutic relationship was also significantly related to acceptance based responding. Participants in the combined condition were more likely to reduce avoidant and inflexible responding to internal states associated with smoking, and accepting and responding more flexibly to these states statistically mediated the effect of the combined treatment on smoking status.

Further research is needed to clarify these results, as the exact nature of the relationship between the alliance and acceptance cannot be determined by the present study, but it suggests that therapeutic relationships may help foster greater acceptance and behavior change. The converse may also be true, and the ARC model identifies reciprocal pathways between acceptance and supportive relationships (Carrico et al., 2007). However, acceptance did not differ significantly between groups at baseline, so it is less likely that this process was responsible for the changes seen in the present study. When relationship and acceptance processes were forced to compete, the critical factor was the degree to which treatment helped smokers accept and respond differently to internal cues linked to smoking.

The current study evaluated whether it was possible for a relationship and acceptance focused behavioral treatment composed of FAP and ACT to improve medication outcomes. The study did not isolate nonspecific effects in either condition. Nor was the study designed to determine whether FAP and ACT are the only cognitive behavioral treatments capable of producing changes in relationship and acceptance. Indeed, from a functional and historical perspective such exclusivity would seem unlikely (Gifford et al., 2006; Hayes, Wilson, Gifford, Follette, & Strosahl, 1996). The study also

Table 6

Bootstrapped (3000 Samples) Point Estimates and Bias Corrected and Accelerated (BCa) Confidence Intervals for the Indirect Effects on 1-Year Smoking Outcomes

	Product of <i>ab</i> Coefficients		BCa 95% CI	
	Point Estimate	SE	Lower	Upper
<i>Individual Mediators</i>				
Smoking-related Acceptance	-.10	.037	-.18	-.04
Therapeutic Relationship	-.17	.084	-.34	-.006
<i>Multiple Mediators</i>				
Smoking-related Acceptance	-.09	.036	-.18	-.03
Therapeutic Relationship	-.12	.077	-.28	.03
Total	-.21	.081	-.39	-.06

did not make comparisons among the interventions comprising ACT and FAP. ACT and FAP are parallel and mutually supportive technologies that share a functional approach to human behavior (Kohlenberg et al., 1993), but it is not clear whether particular aspects of the ACT and FAP interventions were more successful at influencing the processes specified by the model. Further research is needed to identify how best to influence the ARC functional processes (Moos, 2007), including comparing this treatment with other psychosocial treatment options. In a recent small trial of ACT versus CBT for smoking cessation, ACT showed significantly better outcomes than CBT at 1-year follow-up (30% for ACT compared to 13% for CBT; Hernández-López et al., 2009).

There are other limitations to the study. Although a variety of methods obtained the same pattern of results, no statistical method can fully compensate for missing data. Further, the combined treatment was shown to be effective for motivated smokers without active severe depression, anxiety, psychosis, or medical problems contraindicating treatment with bupropion (e.g., head trauma, seizure disorders), so generalizability remains a question. Cost-effectiveness is also an issue due to the intensive nature of the counseling treatment. Recent studies have shown significant effects for brief acceptance-based treatments (e.g., Gregg et al., 2007; Lillis & Hayes, 2008). The present study was designed to identify whether treatment could have an effect; future studies may examine whether less intensive versions achieve similar outcomes. The feasibility of a five-session ACT telephone protocol based on Gifford et al. (2004) has been demonstrated in a recent pilot study (Bricker, Man, Marek, Liu, & Peterson, 2010).

The fact that the AIS predicted outcomes while the AAQ did not is worthy of mention. The AAQ is typically thought of as a general measure of experiential avoidance (Hayes, Strosahl, et al., 2004; Hayes, Wilson, et al., 2004). It may be more sensitive to acceptance interventions in the areas of anxiety and depression as one third of its items are focused on anxiety and depression (according to the instrument developers, these items were derived from the kinds of issues commonly addressed in outpatient ACT treatment). The other AAQ items are more general (e.g., “I often catch myself daydreaming about things I've done and what I would do differently next time”) and may measure general trait factors as opposed to specific avoidance repertoires. The AIS was developed in 2001 in order to capture avoidant and inflexible responding to internal stimuli associated with specific targeted avoidance repertoires such as smoking or compulsive eating (Gifford, 2001;

Gifford et al., 2004). Since that time, these targeted acceptance measures have been shown to be sensitive to change in other populations and have been used in evaluating acceptance interventions for a variety of conditions, including obesity (Gifford & Lillis, 2009) and self-care for diabetics (Gregg et al., 2007). How individuals respond to internal states related to their specific problem behaviors may provide a more sensitive measure of avoidance patterns. The AAQ also showed relatively poor internal consistency in the present study (the brief screening measures also had low alphas, although this is not uncommon, see Ebbert, Patten & Schroeder, 2006, and diagnostic interviews and other study procedures provided checks on accuracy).

Given the lack of meaningful data on specific mediational processes from traditional “horse race” studies, the field has called for the development of behavioral models specifying process-outcome relationships (e.g., Niaura & Abrams, 2002). A primary strength of the present study is its focus on functional process, using a specific behavioral model to guide development of a treatment targeting specified proximal outcomes. The present findings, along with others, suggest the benefits of expanding smoking treatment from its historical focus on reducing or removing aversive symptoms (e.g., through medication alone) to help smokers accept and respond flexibly to these experiences when they occur.

Although proximal outcomes at posttreatment statistically mediated distal outcomes at 1-year follow-up (Finney, 1995; Finney, Moos, & Humphreys, 1999), in future it will be important to assess when during treatment these process changes occur. Since the posttreatment outcomes were significantly different, it is not possible to fully rule out the impact of outcomes at this time period (Stice, Presnell, & Gau, 2007). In an earlier study on the AIS as a mediator of acceptance-based treatment smoking-cessation outcomes (Gifford et al., 2004), 1-year follow-up results were significantly different between conditions but not the post- and 6-month follow-up outcomes. One-year results were still mediated by posttreatment AIS levels, suggesting that the direction of the relationship is from the AIS to outcomes and not the reverse. Future research should assess relationship and acceptance processes during treatment to rule out potential confounds. It is also possible that administering a pharmacological agent designed to reduce symptoms may have undermined an acceptance approach, particularly since the effect size for ACT in the previous study without added medication was somewhat larger (Gifford et al., 2004).

Many have argued for the importance of developing new theoretically based behavioral treatment models for smoking cessation treatment (Niaura & Abrams, 2002; Shiffman, 1993). Others have extended this argument to developing models that incorporate the multidimensional nature of smoking (Tiffany, Conklin, Shiffman, & Clayton, 2004). The present study indicates that functional approaches such as the ARC model may provide a useful theoretical framework for developing combined treatments for smoking, and that behavioral treatments such as the mutual use of FAP and ACT have an important contribution to smoking cessation above and beyond the effects of medication.

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