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RESEARCH PAPER

Differential medication attitudes to antihypertensive and mood stabilizing agents in response to an automated text-messaging adherence enhancement intervention

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Abstract Individuals with serious mental illnesses such as bipolar disorder (BD) are at an increased risk for poor medication adherence compared to the general population. Individuals with BD also have high rates of chronic comorbid medical conditions like hypertension (HTN), diabetes, and cardiovascular disease. Cognitive-behavioral therapies often integrate strategies to improve medication adherence by targeting medication attitudes and self-efficacy, but the pathway toward behavior change needs further investigation. This 3-month prospective, single-arm cohort study tested an automated SMS intervention entitled *Individualized Texting for Adherence Building-Cardiovascular* (iTAB-CV) in 38 participants with BD and HTN. The Tablets Routine Questionnaire (TRQ) measures the percentage of BD and HTN non-adherence over the past week and the past month. Attitudinal and habit measures including the Brief Illness Perception Questionnaire (Brief IPQ), the Medication Adherence Self-Efficacy Scale-Revised (MASES-R), the Self-Report Habit Index (SRHI), the Beliefs about Medicines Questionnaire (BMQ), and the Attitudes toward Mood Stabilizers Questionnaire (AMSQ) were given for BD and HTN medications. Correlational analyses were run to determine the associations between BD and HTN attitudinal and habit indices. Additionally, longitudinal analyses were conducted to determine if attitudes

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changed over time as a function of a 2-month mobile-health intervention. Illness attitudes towards BD were worse than towards HTN at the start of the study. Attitudes toward BD and towards mood-stabilizing drugs as well as antihypertensives improved following a mHealth intervention aimed at improving adherence. Furthermore, self-efficacy and habit strength for both BD and HTN drugs were correlated and were responsive to the intervention, with most of the change occurring after the first month of the intervention and not requiring the addition of the explicit reminders. Participants who received iTAB-CV showed improved attitudes towards BD and mood-stabilizing medication, and had an improvement in self-efficacy and habit strength towards taking both BD and HTN medications. Increased attention to mechanisms of change in mHealth interventions for adherence may facilitate impact. It should be noted that the methodology of the study limits drawing causal conclusions and suggests the need for a randomized control trial.

Introduction

Treatment adherence is defined as the individual's ability to follow through with a health care provider's prescribed treatment (Leclerc, Mansur, & Brietzke, 2013). Individuals with a mental illness such as bipolar disorder (BD) are at an increased risk for poor medication adherence compared to the general population(Azadforouz, Shabani, Nohesara, & Ahmadzad-Asl, 2016; Chakrabarti, 2016; Chapman & Horne, 2013) and not taking one's prescribed medication can have serious consequences. Non-adherence has been linked to an increase in suicidality, mortality, hospitalization, and poor health outcomes (MacDonald, Chapman, Syrett, Bowskill, & Horne, 2016). In fact, non-adherent individuals with BD are over five times more likely to attempt suicide than individuals who are adherent (Miklowitz & Johnson, 2006).

Suboptimal adherence is a complex and multifaceted public health issue occurring among millions of individuals worldwide (Costa et al., 2015). Non-adherence can occur intentionally (i.e. the individual makes a choice not to take the medicine) or unintentionally (e.g. the individual forgets or has cognitive impairment that impacts one's ability to organize and follow through with medication-taking behavior) (Leclerc et al., 2013). Non-adherence has many risk factors, including fear of side effects, the high cost of medication, forgetfulness, health literacy barriers, or the inability to understand the severity of their illness (Krivoy et al., 2015). Non-adherence is also associated with age (particularly worse in the very young and the very old), type of medical condition and treatment, socioeconomic status, and education (Geboers et al., 2015; Krivoy et al., 2015).

The prevalence and relative risk of several chronic medical conditions, such as diabetes, obesity, CVD, HTN, and metabolic syndrome are much higher in the BD population (De Hert et al., 2011). These comorbidities significantly increase disease burden, financial costs, and cause premature mortality (Cutler, Fernandez-Llimos, Frommer, Benrimoj, & Garcia-Cardenas, 2018; Hsu, Chien, & Lin, 2015; De Hert et al., 2011). Evaluating the relationship between medication attitudes and adherence to medications for physical and mental health has the potential to provide valuable information and thus may lead to improving outcomes in this challenging population. When looking at BD and HTN specifically, the literature is sparse but suggests that patient attitudes may differ (Croghan et al., 2003; Sansone, Dunn, Whorley, & Gaither, 2003) and could be affected by several factors, including personal beliefs, stigma, perception of illness severity, education, and motivation (Chang, Sajatovic, & Tatsuoka, 2015; Gerlach & Larsen, 1999). Furthermore, attitudes toward psychotropics may be more affected by stigma as opposed to antihypertensives (Levin, Aebi, Tatsuoka, Cassidy, & Sajatovic, 2016; Levin, Krivenko, Bukach et al., 2016). While stigma regarding mental illness is well-documented, how it selectively impacts behavior in people with multi-morbidity is less studied.

Emerging research suggests that it is possible to modify adherence behaviors in people with BD using components of cognitive-behavioral therapies (Levin, Krivenko, Howland, Schlachet, & Sajatovic, 2016), however, the mechanisms of action whereby upstream or contributory factors lead to changes in adherence is unclear. An important step in understanding how behavior change may occur over time is to assess key patient factors such as medication attitudes, habit strength, and self-efficacy in response to behavioral interventions intended to promote adherence. These data stem from a pilot trial of a mobile-health intervention, based on cognitive-behavioral principles, intended to improve medication adherence assess the associations between attitudes, habit strength and self-efficacy in a sample of individuals with BD and HTN. We hypothesized that attitudes, habit strength, and self-efficacy would all improve over time with an intervention focused on improving adherence with BD and HTN medications.

Methods

Study description

The study from which these data are derived was a 3-month prospective single-arm cohort study which tested an automatic SMS intervention entitled *Individualized Texting for Adherence Building-Cardiovascular* (iTAB-CV) in 38 poorly

adherent individuals with BD and HTN. These individuals were being treated with an evidence-based antihypertensive medication and mood stabilizer and/or antipsychotic medication (Levin et al., 2019). The study used a prospective cohort design with the participants serving as their own control during the course of the 3-month study. Study methods are described in detail elsewhere (Levin et al., 2019). The primary findings of the pilot report were that participants with BD and HTN were highly engaged in the intervention, and both treatment adherence and blood pressure improved (Levin et al., 2019).

Individuals who met the eligibility criteria had a 30-day run-in period where their medication adherence was measured with the Tablets Routine Questionnaire (TRQ) (Adams & Scott, 2000). Following the run-in period, participants received psychoeducation on the symptoms, risks, and important role of medication in the treatment of HTN and BD. They also received a mobile phone and training on how to use and respond to the iTAB-CV messages. In Stage 1 of iTAB-CV, which lasted one month, participants received: 1) alternating daily texts with psychoeducational and motivational content and 2) a daily question assessing mood. In Stage 2, which lasted one month, participants received daily texts which included medication reminders, contextual cues, and immediate positive reinforcement for medication-taking behavior. Prior to the start of the text-messaging intervention, participants were given the opportunity to eliminate content areas and create personalized content. The online supplement for the primary outcomes mauscript gives examples of text content (Levin et al., 2019). Assessments included evaluation of treatment adherence, self-efficacy for medication-taking behavior, illness beliefs, medication attitudes, and habit strength for both HTN and BD medications. These scales were completed at Screen, Visit 1 (V1) at 8 weeks and Visit 2 (V2) at 12 weeks (See Table 2).

Participants and recruitment

Study participants were recruited from the local community. Inclusion criteria included: 1) being at least 18 years of age, 2) a diagnosis of both HTN and BD as confirmed by the Mini International Psychiatric Inventory (M.I.N.I.) version 6.0 (Sheehan et al., 1998), 3) an average systolic blood pressure (BP) reading of 130 or greater based on 3 readings, and 4) having poor adherence to their oral antihypertensive as defined by missing at least 20% of their medication in the past week or month on the TRQ. The study was approved by the local IRB and written informed consent was obtained.

Measures

Adherence measures

Tablets Routine Questionnaire (TRQ)

Adherence was assessed using the TRQ for both HTN and BD medications separately. The TRQ is a self-report measure which identifies non-adherence for the past 7 and past 30 days (Adams & Scott, 2000). The TRQ measures the percentage of days with missed doses of a given medication. Adherence was assessed for each regularly-scheduled HTN medication prescribed. An average HTN TRQ was calculated for participants who were on more than one HTN medication. Similarly, an average BD TRQ was calculated for individuals taking more than one regularly-scheduled BD medication.

Attitude measures

The Brief Illness Perception Questionnaire (Brief IPQ)

The Brief IPQ is a nine-item self-report questionnaire that provides a quick assessment of illness perceptions (Broadbent, Petrie, Main, & Weinman, 2006). Eight items are rated on a ten-point Likert scale, and one question asks the individual to rank factors that contributed to their illness. Total scores range from 0—80, with higher scores indicating a more negative view of the illness.

The Medication Adherence Self-Efficacy Scale-Revised (MASES-R)

The MASES-R is a 13-item questionnaire that measures one's confidence to adhere to their HTN medication regimen under various challenging conditions (Fernandez, Chaplin, Schoenthaler, & Ogedegbe, 2008). Each item's score ranges from 1—4. The total score also ranges from 1—4, as it is calculated by averaging all 13 items. Higher scores indicate a higher self-efficacy. The MASES-R was also adapted for use in BD.

The Beliefs about Medicines Questionnaire (BMQ)

The BMQ is an 18-item measure which is strategically split into two sections (Horne, Weinman, & Hankins, 1999). The first section (BMQ General; 8 items) addresses the participant's beliefs regarding medication in general and the second section (10 items) focuses on the participant's beliefs about their own prescribed medications. Each item is measured on a five-point Likert scale. The general scale has a total score which ranges from 8 to 40, and the medication-specific scale has a total score which ranges from 10—50. In this study, the BMQ General scale was given and the second section was given for HTN medications and BD medications, separately.

The Self-Report Habit Index (SRHI)

The SRHI is a 12-item self-report questionnaire that measures the strength of an individual's medication-taking habit (Verplanken & Orbell, 2003). Specifically, the SRHI includes questions which assess the repetition or automaticity of the participant's medication-taking behavior. This study utilized the SRHI for both BD and HTN medications. Each item is scored from 1—7 and item scores are averaged to get a total score. Higher values indicate stronger habits.

The Attitude toward Mood Stabilizers Questionnaire (AMSQ)

The AMSQ is a modification of the Lithium Attitudes Questionnaire. The AMSQ is a 19-item measure which evaluates an individual's attitudes towards mood stabilizers (Chang et al., 2015). Total scores range from 0 to 19; higher total scores indicate more negative attitudes. The measure was adapted to evaluate attitudes towards antihypertensives.

Data analysis

Analyses were run using the Statistical Package for Social Sciences (SPSS), version 24.0. One-way repeated measures of variance (ANOVAs) were run to analyze change in attitudes, habit strength, self-efficacy, and illness/medication beliefs across the study timeline. ANOVAs were run for both HTN and BD variants of each scale. Post-hoc analyses used a Bonferroni correction. Pearson correlations were run at each time point (Screen, V1, V2) for each attitudinal measure comparing HTN to BD (e.g. correlating Brief IPQ HTN at screen with Brief IPQ BD at screen). Due to non-normality of the adherence data, Spearman correlations were run to determine if the Brief IPQ, MASES-R, BMQ, SRHI, and AMSQ significantly correlated with past-week HTN TRQ or past-week BD TRQ ($n = 37$) at each time point. There were no missing data aside from one participant who did not complete past-week BD TRQ.

Results

Overall

Sample demographic characteristics are presented in Table 1. Mean age was 51.53 (SD = 9.06) years; 20 (52.6%) were female, 28 (73.7%) were African American, 15 (52.6%) were single/never married, and average years of education was 13.18 years (SD = 2.69). Twenty-six (68.4%) participants had at least one psychiatric hospitalization in their lifetime, and nineteen (50.0%) had at least one HTN-related hospitalization in their lifetime. Twelve (31.6%) participants had at least one substance use hospitalization in their lifetime. The majority of the sample was disabled (73.7%) or unemployed but expected to work (15.8%). The large majority of the sample had Medicaid insurance (73.7%).

Table 1 Demographic characteristics of study sample at screen.

Variable	Mean or *n*	SD or %
Age	51.53	9.06
Female	20	52.6%
Marital status		
Single/never married	20	52.6%
Married	3	7.9%
Separated/divorced/widowed	15	39.5%
Race		
African-American	28	73.7%
Caucasian	9	23.7%
Other	1	2.6%
Hispanic	2	5.3%
Years of education	13.18	2.69
Employment		
Full time/homemaker	1	2.6%
Part time	3	7.9%
Unemployed, but expected to work by self or others	6	15.8%
Disabled	28	73.7%
Insurance type[a]		
Medicaid	28	73.7%
Medicare	11	28.9%
Private	0	0.0%
No insurance	0	0.0%
Other	6	15.8%
Bipolar disorder type		
BD I	28	73.7%
BD II	10	26.3%
Age of hypertension (HTN) Diagnosis	36.95	15.66
Age of bipolar disorder diagnosis	31.95	13.46
Lifetime HTN-related hospitalizations		
Yes	19	50.0%
If yes, how many? Median, range	3.16	Range 1—15
Lifetime psychiatric hospitalizations		
Yes	26	73.7%
If yes, how many? Median, range	3.00	Range 1—30
Smokes cigarettes		
Yes	23	60.5%
If yes, how many cigs per day? Median, range	6.00	Range 1—20
Body Mass Index (BMI)	22.15	9.40

[a] Categories are non-exclusive.

Attitudes

As noted in Table 2, there was a significant difference in Brief IPQ BD scores between screen (SCR) and V1 and SCR and V2 ($F(2,74) = 6.90$, $p = 0.002$). The MASES-R yielded similar results with a significant difference in both BD ($F(1.5, 56.3) = 21.14$, $p < 0.001$) and HTN scores ($F(1.6, 58.6) = 30.30$, $p < 0.001$) between screening and V1 and screening and V2. The SRHI also shows a significant difference in BD scores ($F(1.5, 55.1) = 9.74$, $p < 0.001$) between screening and V1 and screening and V2. Regarding HTN, the SRHI shows improvement in scores between all combinations of time points except for between V1 and V2. The AMSQ shows improvement in scores for both HTN and BD between screening and V1 and screening and V2.

Comparing HTN to BD on each attitudinal and habit strength measure, the following scales were significantly correlated at each time point: MASES-R, SRHI, and the AMSQ (all p values < 0.03). The Brief IPQ was significantly correlated between BD and HTN at screen ($r_s(36) = 0.39$, $p = 0.02$) yet was not significantly correlated at V1 or V2 (both p values > 0.08).

Adherence

Correlations between HTN TRQ and each of the attitudinal measures at each time point yielded no significant correlations between HTN TRQ and Brief IPQ at screen, V1, or V2 (all p values > 0.44). Similarly, there were no significant correlations between HTN TRQ and BMQ at screen, V1, and V2 (all p values > 0.26). There were, however, significant correlations between HTN TRQ and the SRHI at screen ($r_s(36) = -0.40$, $p = 0.012$), V1 ($r_s(36) = -0.43$, $p < 0.01$) and V2 ($r_s(36) = -0.44$, $p < 0.01$),

Table 2 One-way ANOVAs assessing attitude measures across time for hypertension and bipolar medications separately ($n = 38$).

	Screen Mean (SD)	Baseline Mean (SD)	V1 Mean (SD)	V2 Mean (SD)	Statistic*
Brief IPQ[a]					
HTN	44.92 (11.5)	—	41.63 (10.38)	41.84 (11.11)	$F(2, 74) = 1.92$, $p = 0.15$
BD	52.58 (9.69)	—	48.39 (11.07)	47.84 (9.40)	**$F(2, 74) = 6.90$, $p = 0.002$,** $\eta_p^2 = 0.16$
MASES-R[b]					
HTN	2.35 (0.54)	—	2.98 (0.62)	3.04 (0.57)	**$F(1.6, 58.6) = 30.30$, $p < 0.001$** $\eta_p^2 = 0.45$
BD	2.32 (0.73)	—	2.98 (0.75)	2.97 (0.74)	**$F(1.5, 56.3) = 21.14$, $p < 0.001$,** $\eta_p^2 = 0.36$
BMQ[c]					
HTN	36.24 (5.70)	—	34.55 (5.70)	34.42 (5.27)	$F(1.7, 62.6) = 3.07$, $p = 0.06$
BD	34.34 (5.25)	—	34.03 (4.73)	34.87 (5.29)	$F(1.4, 51.3) = 0.58$, $p = 0.51$
General	23.22 (6.09)	—	22.78 (5.59)	22.17 (5.33)	$F(2, 70) = 1.30$, $p = 0.28$
SRHI[d]					
HTN	3.60 (1.01)		4.91 (1.28)	5.17 (1.13)	**$F(1.7, 62.3) = 42.80$, $p < 0.001$,** $\eta_p^2 = .54$ **$F(1.5, 55.1) = 9.74$, $p < 0.001$,** $\eta_p^2 = .21$
BD	4.08 (1.24)		4.93 (1.45)	4.98 (1.41)	
AMSQ[e]					
HTN	7.92 (3.51)	—	4.11 (2.84)	3.26 (2.76)	**$F(1.7, 62.9) = 60.91$, $p < 0.001$** $\eta_p^2 = 0.62$
BD	7.82 (4.37)	—	4.74 (3.80)	4.47 (3.69)	**$F(2, 74) = 19.01$, $p < 0.001$,** $\eta_p^2 = 0.34$

Bold indicates statistical significance.

* $0.01 \leq \eta_p^2 < 0.06$ = small effect size; $0.06 \leq \eta_p^2 < 0.14$ = medium effect size; $\eta_p^2 \geq 0.14$ = large effect size.

[a] Brief IPQ: Brief Illness Perception Questionnaire. Total scores range from 0—80, with higher scores indicating a more threatening view of the illness.

[b] MASES-R: The Medication Adherence Self-Efficacy Scale. Each item's score ranges from 1—4. Total score also ranges from 1—4, as it is calculated by averaging all 13 items. Higher scores indicate a higher self-efficacy.

[c] BMQ: Beliefs about Medicines Questionnaire. The general scale has a total score which ranges from 8 to 40, and the medication-specific scale has a total score which ranges from 10—50. Higher scores indicate a worse perception of medication.

[d] SRHI: Self-Report Habit Index. There are 12 items on the SRHI, each scores from 1—7. Scores are averaged to get a total score. Higher values indicate stronger habits.

[e] AMSQ: Attitude toward Mood Stabilizers Questionnaire. Total scores range from 0 to 19; higher total scores indicate a more negative attitudes.

and a trend at BL ($r_s(36) = -0.32$, $p = 0.053$). There were significant correlations between HTN TRQ and the MASES-R at V1 ($r_s(36) = -0.42$, $p < 0.01$) and V2 (V2 $r_s(36) = -0.50$, $p = 0.001$), but not at screen ($p > 0.48$). There were significant correlations between past week HTN TRQ at screen and HTN AMSQ at screen ($r_s(36) = 0.51$, $p = 0.001$) and V1 ($r_s(36) = 0.46$, $p = 0.004$). There was a trending significant correlation between past week HTN TRQ and HTN AMSQ at V2 ($r_s(36) = 0.31$, $p = 0.057$). Finally, there were no significant correlations between past week BD TRQ and BD AMSQ BD at screen or V1 (both p values > 0.13). However, there was a significant correlation between BD non-adherence and BD AMSQ at V2 ($r_s(36) = 0.41$, $p = 0.01$).

Discussion

This analysis, derived from a pilot study of poorly adherent patients with BD and HTN participating in the iTAB-CV intervention, which is based on cognitive-behavioral principles, found several significant associations between perceptions of illness, medication attitudes, habit strength, and adherence behaviors. Findings are potentially important given the high rates of poor adherence typically associated with both BD and HTN and the negative health outcomes associated with poor adherence, which lead to premature mortality in this and similar populations (Crump, Sundquist, Winkleby, & Sundquist, 2013).

At study screen, participants appeared to perceive their BD more negatively than their HTN. The difference in perceptions toward BD compared to HTN may be because the observed and felt negative effects of BD are obvious and affect daily functioning in comparison to HTN which does not cause clinical symptoms or functional impairment until individuals develop complications such as heart attack or stroke. An alternative explanation for the more negative attitudes towards BD vs. HTN is self-stigma, in which an individual with mental illness internalizes the stigma and then experiences diminished self-esteem. This process limits its prospects for recovery. Social psychologists suggest this process begins even before the person is afflicted with mental illness because it is during that period that he/she usually learns about and internalizes culturally disseminated stereotypes about such illnesses (Rössler, 2016). Our pilot results suggest that attitudes towards BD significantly improved as a function of receiving the iTAB-CV mHealth intervention. This is consistent with other studies which have found that interventions with elements of psychoeducation improve attitudes towards having BD or other serious mental illness (Bauer et al., 2006; Levin et al., 2014).

The Attitude-Social Influence-Efficacy (ASE) explanatory model upon which iTAB-CV was based consists of 3 cognitive components that predict behavioral intent and change: attitude (A), social influence (S), and self-efficacy (E). Attitude encompasses perceived advantages and disadvantages to adherence; social influence addresses perceived norms, social support, and modeling of adherence behavior; self-efficacy refers to the individual's belief about their ability to achieve adherence. In our sample, attitudes toward illnesses (BD and HTN), attitudes toward medication (BD medication and HTN medication), self-efficacy for medication taking behavior, and habit strength for medication taking were for the most part significantly associated with each other. Furthermore, as a whole, participants who started the study with negative attitudes toward BD/BD medications also had negative attitudes toward HTN/HTN medications. Participants increased their self-efficacy for being able to take their medications regularly for both BD and HTN medications and strengthened their habit of taking both BD and HTN medications in response to iTAB-CV.

It is notable that while illness attitudes towards BD, attitudes about taking medication, self-efficacy for medication taking, and habit strength improved throughout the study for both BD and HTN, the largest change occurred following the 1st month of the mHealth intervention and was then maintained in the 2nd month. To understand this finding, one must look at how the elements in months one and two were different. While in month one, all participants received 1 psychoeducational/motivational text in the first part of the day without an explicit medication reminder, in month 2 they received up to 4 such texts, with an explicit reminder, and delivery at the time that the medicine was to be taken. The addition of explicit reminders in the second month (e.g. ''time to take meds now'') did not seem to have added value with regard to modifying attitudes nor did the increased frequency of messaging. One might interpret this to suggest that reminders are not important in influencing attitudes. While that is possible, it is more likely that the first month's texts served not only as educational and motivational but also as implicit reminders even though they were not intended to do so. As such, it does not appear than an explicit reminder is necessary to change medication attitudes and the optimal number of texts to achieve attitude change has yet to be determined. In fact, when taking into account the burden of multiple texts per day, if the results are attained with fewer texts, that is likely to be preferable to participants (Finitsis, Pellowski, & Johnson, 2014).

Regarding medication adherence, there was no significant relationship between adherence to HTN medications and negative illness beliefs. Furthermore, perception about the dangers of medication (i.e. that they are harmful, addictive, or should not be taken continuously) for both BD and HTN medications did not change throughout the study which may suggest that one's cognitive representation for medication is different than one's belief in the need for the medication. Building medication-taking into one's routine (habit strength) is seen in the context of better adherence and is illustrated by the significant correlations between adherence and habit strength at each time point.

Limitations of the study include the absence of a control group, the single-site setting, a relatively small study sample, short duration (3 months), and the use of subjective adherence and attitude measures. Offsetting these limitations is the notable strength of having a large proportion of African-Americans who are often underrepresented in research studies and have higher rates of HTN (Lewis, Ogedegbe, & Ogedegbe, 2012; Mozaffarian et al., 2016), worse medication adherence (Charles, Good, Hanusa, Chang, & Whittle, 2003), and worse health outcomes (Lewis et al., 2012; Poon, Lal, Ford, & Braun, 2009).

Conclusion

Participants who received iTAB-CV showed improved attitudes towards BD and mood-stabilizing medication, had an improvement in self-efficacy and developed a stronger habit of taking both BD and HTN medications. Interventions that concurrently address mental and physical health may help address impediments to recovery in people with BD who have complex medical conditions. However, in order to confirm this conclusion, several steps are in order. First, randomized controlled trials are needed to establish efficacy followed by more sophisticated adaptive designs such as micro-randomized trials which aim to provide the needed treatment components at the correct time for a given person. Additionally, future research should use a larger sample and conduct a mediational analysis in order to establish the possible mechanism of attitude change.

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Disclosure of interest

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