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Cognition-emotion interactions are modulated by working memory capacity in individuals with schizophrenia

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ABSTRACT

Prior research provides evidence for aberrant cognition-emotion interactions in schizophrenia. In the current study, we aimed to extend these findings by administering the “distractor devaluation” task to 40 individuals with schizophrenia and 32 demographically matched healthy controls. The task consisted of a simple visual search task for neutral faces, followed by an evaluative response made for one of the search items (or a novel item) to determine whether prior attentional selection results in a devaluation of a previously unattended stimulus. We also manipulated working memory demands by preceding the search array with a memory array that required subjects to hold 0, 1, or 2 items in working memory while performing the search array and devaluation task, to determine whether the normative process by which attentional states influence evaluative response is limited by working memory capacity. Results indicated that individuals with schizophrenia demonstrated the typical distractor devaluation effect at working memory load 0, suggesting intact evaluative response. However, the devaluation effect was absent at working memory loads of 1 and 2, suggesting that normal evaluative responses can be abolished in people with schizophrenia when working memory capacity is exceeded. Thus, findings provide further evidence for normal evaluative response in schizophrenia, but clarify that these normal experiences may not hold when working memory demands are too high.

1. Introduction

There has been a resurgence of interest in the area of emotional functioning in schizophrenia (Kring and Moran, 2008). Much of this work has focused on the nature of emotional experience in response to standard stimuli such as pictures, movies, smells, and film clips (Berenbaum and Oltmanns, 1992; Kring et al., 1993; Earnst and Kring, 1999; Horan et al., 2006; Strauss and Herbener, 2011). While there are exceptions (e.g., Strauss et al., 2010a), most studies indicate that patients and healthy controls report experiencing a similar magnitude of positive emotion when exposed to positive stimuli (see Cohen and Minor, 2010 for a meta-analysis), thereby challenging traditional concepts of anhedonia as a diminished capacity for pleasure (see Strauss and Gold, 2012 for a new perspective). However, it is clear that not all aspects of emotional experience are normal in schizophrenia. For example, patients also report increased levels of negative emotion in response to neutral and pleasant stimuli (see Trémeau et al., 2009; Cohen and Minor, 2010) and display reductions in pleasure-seeking and goal-directed behavior (Gard et al., 2007; Foussias and Remington, 2010; Oorschot et al., in press). Thus, an important question remains to be answered: why is it that patients' intact ability to experience emotions does not result in motivated behavior?

One possibility is that dysfunctional cognition-emotion interactions prevent these intact emotional experiences from being translated into motivated, goal-directed actions. Individuals with schizophrenia display a range of abnormalities in cognition–emotion interactions, and these have often been linked to greater severity of negative symptoms, particularly anhedonia and avolition. For example, patients display impairments in long-term emotional memory (Herbener et al., 2007; Herbener, 2008), emotional working memory capacity and maintenance (Anticevic et al., 2011; Gard et al., 2011; Kring et al., 2011; Ursu et al., 2011), reward learning (Waltz and Gold, 2007; Waltz et al., 2007; Gold et al., 2008; Strauss et al., 2011a,c; Gold et al., 2012), and dysfunctional emotion-attention interactions (Kinderman et al., 2003; Strauss et al., 2008; Besnier et al., 2011; Strauss et al., 2011b). The aforementioned studies have primarily investigated how emotional stimuli interact with cognition. However, in healthy individuals, it is known that the reverse is also possible, i.e., basic cognitive processes can influence subjective emotional experience and evaluative response. Given the nature and severity of cognitive impairment in schizophrenia (Heinrichs and Zakzanis, 1998), there is reason to suspect that cognitive processes may not influence evaluative response normally when cognitive demands are high.

The “distractor devaluation” paradigm may offer a novel means of testing this possibility and extending the literature on cognition–emotion interactions in schizophrenia (Fenske et al., 2004; Raymond

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et al., 2005; Goolsby et al., 2009). In this task, participants perform two procedures. First, they are asked to complete a simple attentional visual search task (e.g., two faces are presented on the screen, one male and one female, which are tinted in red or blue hue. Participants are given the task of identifying the color in which the male faces, the search target, are tinted). Then, on a subsequent screen, they make an evaluative response in relation to one of the search items (or a novel item) to determine whether prior attentional selection results in differences in evaluative response to the previously attended or unattended stimulus (e.g., subjects see a single neutral face that was either a target in the search array or a novel face and rate it on trustworthiness using a 1–9 scale). Studies using this paradigm consistently indicate that this attentional selection manipulation influences subsequent evaluative responses, whereby healthy people devalue (i.e., give lower ratings) stimuli that they have been led to ignore (i.e., distractors) on the basis of task instructions relative to stimuli that have been subjected to selective attention (i.e., targets).

An inhibition-based theory has been applied to explain this effect. When multiple stimuli are in competition for selective attention, inhibitory processes are enacted and then associated with the mental representation of the stimuli that were unattended (Raymond et al., 2003; Tipper et al., 2003; Kessler and Tipper, 2004). When an unattended stimulus is subsequently presented, the inhibitory processes are re-evoked, causing the unattended stimulus to be emotionally devalued relative to an attended target. Interestingly, the distractor devaluation effect is modulated by working memory, such that healthy subjects show devaluation in the absence of working memory demands and when demands are low to moderate, but fail to show devaluation at higher loads when capacity is exceeded (Goolsby et al., 2009). This has been explained by the fact that at higher loads, processing capacity is fully engaged by the central task, which prevents resources from being devoted to the inhibitory processing that produces the devaluation effect. Thus, attentional selection implicitly influences evaluative response, but this influence may be diminished when working memory demands are too high.

In the current study, we employed the distractor devaluation paradigm to examine cognition-emotion interactions in schizophrenia, and manipulated working memory load to determine whether working memory capacity differentially influences evaluative response in patients relative to controls. We hypothesized that patients would show normal distractor devaluation in the absence of working memory demands (i.e., lower ratings for prior distractors relative to targets), but expected patients to fail to show devaluation at higher loads. Such a pattern of findings would suggest that evaluative processes are normal in people with schizophrenia, but interact with other cognitive deficits and break down under cognitively demanding situations.

2. Methods and materials

2.1. Participants

Participants included 40 patients meeting DSM-IV criteria for Schizophrenia (SZ) and 32 Healthy Controls (CN). Persons with Schizophrenia were recruited through the Outpatient Research Program at the Maryland Psychiatric Research Center, and evaluated during a period of clinical stability evinced by no changes in medication type or dosage for a period greater than or equal to four weeks. Consensus diagnosis was established via a best-estimate approach based upon multiple interviews and a detailed psychiatric history. This diagnosis was subsequently confirmed using the Structured Clinical Interview for DSM-IV (SCID). All SZ participants were taking antipsychotic medication at the time of treatment (see Table 1 note).

Control subjects were recruited by means of random digit dialing, word-of-mouth among recruited participants, and through the use of newspaper advertisements. Controls had no current Axis I or II diagnoses as established by the SCID (First et al., 1997) and SID-P (Pfohl et al., 1997), no family history of psychosis, and were not taking psychotropic medications. All participants denied a history of significant neurological injury or disease, and significant medical or substance use disorders within the last six months. Participants were routinely screened for substance use by means of urine toxicology upon admission to the subject pool, and in any instance where substance use was suspected. All participants provided informed consent for a protocol approved by the University of Maryland Institutional Review Board.

Table 1
Demographic and clinical characteristics of controls (CN) and persons with Schizophrenia (SZ).

	CN ($n=32$)	SZ ($n=40$)
Age	40.41 (10.14)	40.17 (10.41)
Parental education	13.31 (1.91)	13.6 (2.53)
WASI estimated IQ	114.25 (11.50)	92 (13.29)
WTAR SS	108.94 (12.04)	94.85 (14.48)
% male	62.5	57.5
Ethnicity		
American Indian/Alaskan native	0.0%	2.50%
Black/African American	37.50%	37.50%
Mixed race	3.10%	0.0%
White	59.40%	60.00%
MATRICS battery		
Processing speed	54.16 (8.47)	34.28 (12.94)
Working memory	50.03 (9.72)	35.69 (10.71)
Verbal learning	53.47 (12.19)	36.08 (10.41)
Visual learning	47.88 (11.32)	30.82 (14.04)
Social cognition	56.41 (7.80)	38.85 (11.51)
Attention/vigilance	53.53 (8.20)	38.58 (11.87)
Reasoning/problem solving	53.34 (9.89)	40.73 (10.50)
Overall	54.09 (9.32)	28.5 (13.14)

Note. WASI Estimated IQ = Wechsler Abbreviated Scale of Intelligence full-scale estimated IQ; WTAR SS = Wechsler Test of Adult Reading (WTAR) scaled score. Patients were prescribed various antipsychotic medications, either alone (clozapine: n = 15; risperidone: n = 6; olanzapine: n = 4; fluphenazine: n = 3; aripiprazole: n = 1; haloperidol: n = 1; quetiapine: n = 1; thiothixene: n = 1; ziprasidone: n = 1) or in combination with another antipsychotic (risperidone and clozapine: n = 2; aripiprazole and haloperidol: n = 1; olanzapine and clozapine: n = 1; paliperidone and qutiapine: n = 1; clozapine and aripiprazole: n = 1; olanzapine and risperidone: n = 1).

Controls and SZ participants did not significantly differ in age: $F(1,72)=0.01$, $p=0.93$, parental education: $F(1,72)=0.29$, $p=0.60$, gender: X^2 $(1,72)=0.19$, $p=0.67$, or ethnicity: X^2 $(3,72)=2.05$, $p=0.56$. Patients had lower Wechsler Abbreviated Scale of Intelligence (WASI) estimated full-scale intelligence quotients, $F(1,72)=56.10$, $p<0.001$, and lower scores on all MATRICS battery composite scores (all $ps>0.001$) (see Table 1).

2.2. Distractor devaluation task

In the Distractor Devaluation task, participants were asked to complete three primary procedures per trial: working memory encoding and recall, visual search, and evaluative response (see Fig. 1 for sample trial sequence). Each trial began with a 2000 ms working memory array, which was to be remembered by the participant. Images included in the working memory array were a neutral grayscale male face, a neutral grayscale female face, or a placeholder. Placeholders were created by scrambling grayscale facial images into a 20×20 grid (see Fig. 1 for an example). In conditions where working memory load was high (WM-2 conditions) both images were faces. In moderate memory load conditions (WM-1) one image was a face and the other a placeholder. In conditions without working memory load (WM-0) both images were placeholders (see Fig. 1). The working memory array was followed by a 1000 ms retention interval during which a blank screen was displayed. Then a search display appeared, consisting of two faces, one male and one female, which were presented in different hue for 300 ms. Participants were asked to make a dichotomous judgment and identify whether a male or the female face (gender pre-specified) was presented in blue or red tint, as quickly and accurately as possible via button press. The to-be-identified gender remained constant within the experimental

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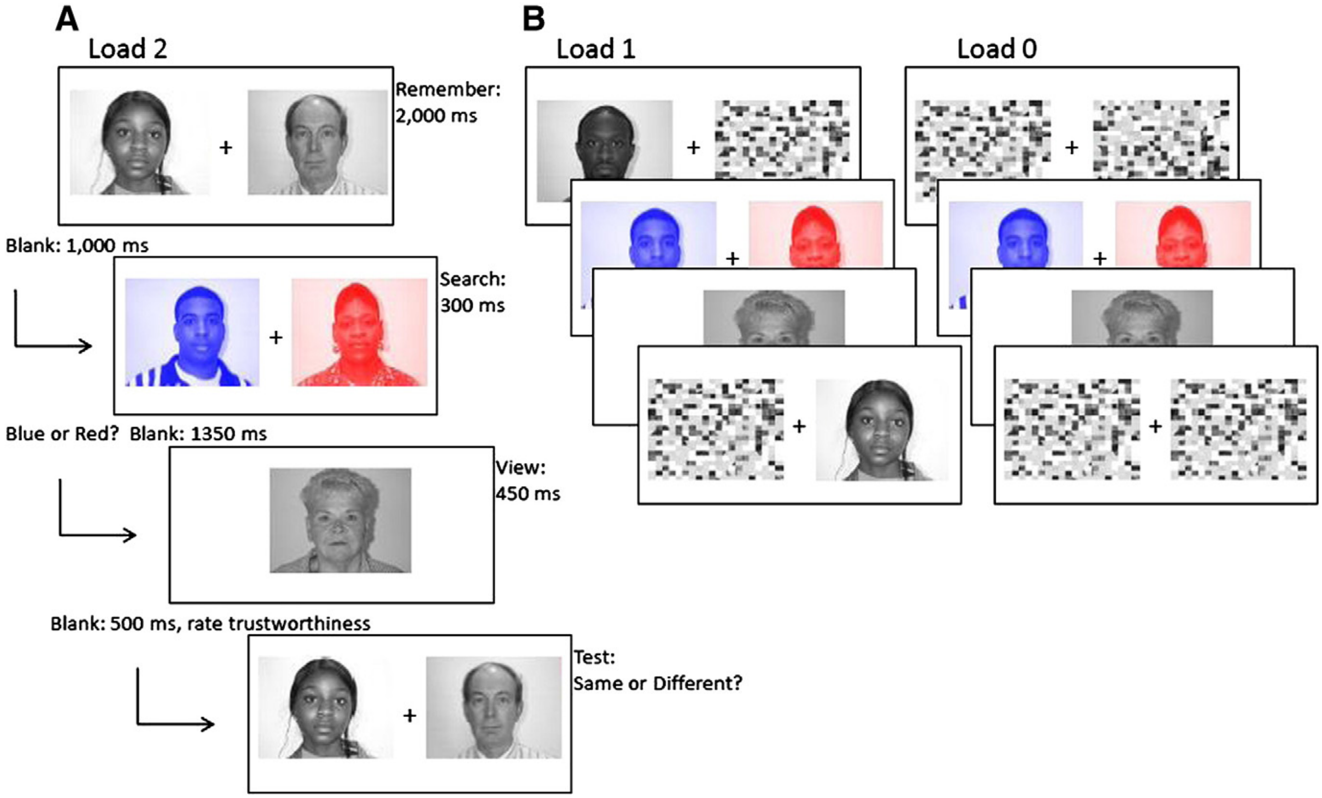

Fig. 1. Diagram of distractor devaluation trial sequence.

block, and there were two experimental blocks presented. The order of the pre-specified target gender was randomized across participants. Following the search array, there was a blank screen for 1350 ms, followed by an evaluative response phase, where participants rated a single grey-scale face that appeared for 450 ms. Similar to prior distractor devaluation experiments (e.g., Raymond et al., 2003; Goolsby et al., 2009), the evaluative response was a judgment of facial trustworthiness on a 1–9 Likert-type scale (1 = not at all trustworthy; 9 = extremely trustworthy). The image to be rated was either the prior target image (the image of the appropriate gender to the task), a prior distractor image, or a novel image not previously presented. Evaluative response was the critical dependent variable used to evaluate the distractor devaluation effect when analyzed in conjunction with prior stimulus type. After the evaluative response, participants then completed the working memory array retention test, where they were presented with two grayscale images that were either identical to or different from the images they were asked to remember at the beginning of the trial. The response prompt asked them to indicate whether or not the set on the screen was identical to the first set of images at the beginning of the trial.

Stimuli were grayscale images of faces (50% female) taken from the Progressive Aging stimulus set (Minear and Park, 2004). Two pictures (4.1° × 6.0° of visual angle each), positioned 2.7° to the left and right of fixation, comprised each test array. All faces were presented with neutral expressions and visible hair.

2.3. Procedure

The distractor devaluation task was given as part of a larger battery of reward learning measures. Patients also completed a clinical interview after which the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962) and the Brief Negative Symptom Scale (BNSS; Kirkpatrick et al., 2011) were rated. The MATRICS Cognitive Consensus Battery (MCCB) (Green et al., 2004) was administered to index neuropsychological functioning.

3. Results

We first examined basic task performance by comparing SZ and CN participants on search array performance, working memory array accuracy, and evaluative response (see Table 2). One-way ANOVAs indicated that patients were significantly less accurate than controls with regard to search array performance, F $(1, 71) = 21.52$, $p < 0.001$, and total WM recall array performance (i.e., collapsing across loads), F $(1, 71) = 20.12$, $p < .001$. Patients were also significantly less accurate than CN at WM Load 0, F $(1, 71) = 4.43$, $p = 0.039$, WM Load 1, F $(1, 71) = 15.11$, $p < 0.001$ and WM Load 2, F $(1, 71) = 36.03$, $p < 0.001$. However, SZ and CN did not differ on global evaluative ratings (i.e., collapsing across WM load and target condition), F $(1, 71) = 0.25$, $p = 0.62$. Thus, as would be expected, patients showed basic neurocognitive deficits, as indicated by poorer working memory and search array performance.

Two sets of analyses were conducted to evaluate the effects of attentional selection and working memory load on evaluative response. First,

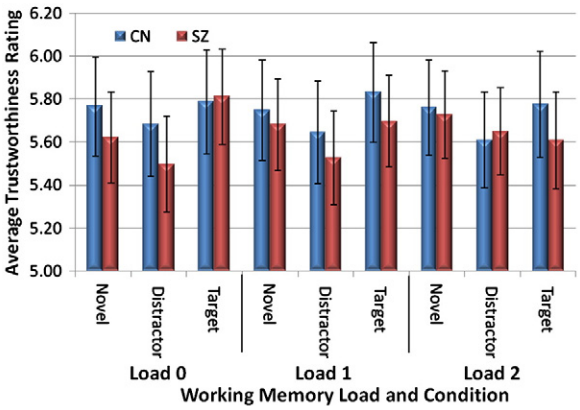

Fig. 2. Distractor devaluation performance in individuals with schizophrenia and controls.

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Table 2
Descriptive statistics for search array and recall array performance in SZ and CN.

	SZ (N = 40)	CN (N = 32)	Test Statistic	p-value
Search array accuracy	88.9%	96.2%	F = 21.52	p < 0.001
Recall array accuracy	71.4%	87.2%	F = 20.12	p < 0.001
WM0 accuracy	75.7%	87.9%	F = 4.43	p = 0.039
WM1 accuracy	73.7%	88.5%	F = 15.11	p < 0.001
WM2 accuracy	66.9%	85.6%	F = 36.03	p < 0.001
Overall trustworthiness	5.61 (1.31)	5.76 (1.07)	F = 0.25	p = 0.62

a 2 group (SZ, CN) × 3 condition (novel, prior target, prior distractor) × 3 working memory load (WM 0, WM 1, WM 2) repeated measures ANOVA was conducted. There was a significant main effect for condition, $F(2, 65) = 4.46$, $p = 0.01$; however, the between-subjects effect of Group, $F(1, 66) = 0.09$, $p = 0.77$, the within-subjects effect of WM Load, $F(1.734, 65) = 0.01$, $p = 0.98$, condition × group interaction, $F(2, 65) = 0.01$, $p = 0.99$, WM load × group interaction, $F(2, 65) = 0.25$, $p = 0.78$, condition × WM load interaction, $F(3.529, 65) = 0.65$, $p = 0.61$, and condition × WM load × group interaction, $F(2, 65) = 0.94$, $p = 0.44$, were all nonsignificant.

Second, to directly test the hypothesized distractor devaluation effect at different WM loads, we conducted a series of within-group paired samples t-tests. In the CN group, there was evidence for devaluing distractors relative to targets at the WM Load 1 condition, $t(1, 30) = -2.17$, $p = 0.04$, and a trend at the WM Load 2 condition, $t(1, 31) = -1.86$, $p = 0.07$, though their distractor and target ratings did not significantly differ at WM Load 0, $t(1, 30) = -0.79$, $p = 0.44$. SZ devalued distractors relative to targets only at WM Load 0, $t(1, 37) = -2.032$, $p < 0.05$ and did not devalue distractors more than targets at WM Load 1, $t(1, 40) = -0.52$, $p = 0.610$, or WM Load 2, $t(1, 40) = -0.305$, $p = 0.76$. Paired-samples t-tests were also used to compare response differences between novel and distractor stimuli in the same fashion as above; no significant effects were observed for these within group contrasts in either group at any of the WM loads (Fig. 2).

To examine distractor devaluation effects independent of WM load, we also conducted paired-samples t-tests on prior target vs. distractor stimuli and novel vs. distractor stimuli for each group (i.e., collapsing across WM loads). CN devalued distractors relative to targets, $t(1, 31) = 2.12$, $p < 0.05$; however, there was no difference between novel and distractor ratings, $t(1, 31) = 1.75$, $p = 0.09$. In SZ patients, there was no significant difference between distractor and target stimuli, $t(1, 39) = 1.39$, $p = 0.18$, or novel and distractor stimuli, $t(1, 39) = 1.81$, $p = 0.08$.

Difference scores were calculated (distractor rating − target rating) to examine the relationship between distractor devaluation and measures of symptom ratings and neuropsychological functioning. At all 3 working memory loads, devaluation scores were not significantly correlated with BPRS scores (positive, disorganized, negative, total), BNSS total or subscale scores, or MATRICS neuropsychological domain scores.

4. Discussion

As hypothesized, individuals with schizophrenia demonstrated the typical pattern of evaluative response in the distractor devaluation task at the working memory load 0 condition. This suggests that attentional selection implicitly influences evaluative processes in a normal way in people with schizophrenia when working memory demands are absent. According to Raymond et al. (2003), the distractor devaluation effect can be explained via an inhibition-based account of the influence of attention on evaluative response. Essentially, when a stimulus inappropriate for the goals of attentional selection (i.e., distractor) competes for control over selection, inhibitory attentional processes are applied and associated with the mental representation of that stimulus (Tipper et al., 2003; Kessler and Tipper, 2004). Subsequently, when the stimulus that was not subject to attentional selection is presented again, this inhibition is reapplied, leading to devaluation of that stimulus relative to an attended target. Given this interpretation, one would conclude that attention influences evaluative response normally in people with schizophrenia in visual search situations where inhibition has been applied. Interestingly, this only appears to be the case when working memory demands are absent. Our findings indicated that although controls demonstrated distractor devaluation even at working memory loads of 1 and 2 (trend-level effect), patients did not devalue distractors more so than targets under load 1 or 2 conditions.

A limitation of our results is that the CN group did not show a statistically robust devaluation of distractors relative to targets at WM Load 0, although the pattern of results was in the predicted direction based upon prior literature. This may have occurred because task parameters were modified from what is commonly used in the basic cognitive neuroscience literature, such that the search array (200 vs 300 ms), evaluative display (300 vs 450 ms), and durations between these displays (1130 vs 1350 ms) were longer. This was done to make the task more valid in patients; however, the result of this modification may have been to cause the WM Load 0 condition to become less cognitively demanding for controls, thereby reducing the magnitude of their devaluation effect at Load 0. Controls did not show systematically lower accuracy in the recall array across loads 0–2, suggesting that the load manipulation was less effective than what was observed by Goolsby et al. (2009). Thus, in terms of cognitive demand, WM load 1 in the current study may have been more akin to WM Load 0 in basic neuroscience studies (Goolsby et al., 2009) for our controls.

A second limitation is that we did not account for basic face perception deficits that are known to affect people with schizophrenia (Kohler and Brennan, 2004; Strauss et al., 2010b). It is therefore unclear whether these deficits contributed to the lack of devaluation at loads 1 and 2 when other cognitive demands were high. Furthermore, the trustworthiness judgments made in the current study are different from the valence and arousal ratings typically made in response to affective stimuli; future studies could extend these findings by having subjects report their subjective feelings to evaluative stimuli. Despite these limitations, these findings are consistent with the notion that cognition-emotion interactions may be abnormal in schizophrenia.

The current findings extend the literature showing that emotional stimuli may not interact with cognitive processes normally in schizophrenia, providing evidence that working memory capacity may interact with attentional selection to determine the extent to which inhibitory processes can promote normal evaluative responses in schizophrenia. It is likely that multiple cognitive impairments contribute to this dysfunction, including cognitive control, attentional selection, working memory, and retrieval- future studies should therefore examine the interaction between affect and multiple cognitive processes.

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Contributors

Gregory P. Strauss and James M. Gold designed the study and wrote the protocol. Data collection was performed by research assistants at the Maryland Psychiatric Research Center. Statistical analysis and writing of the first draft of the manuscript was performed by Gregory P. Strauss and Bern G Lee. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors have no conflicts of interest to report related to this research.

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