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Psychological Medicine, **39** (2009).
doi:10.1017/S0033291709990444
First published online 21 July 2009

Research Letter

High-density negative ion treatment increases positive affective memory

Acute administration of antidepressant drugs which potentiate the activity of serotonin (5-HT) and/or noradrenaline (NA) produces positive biases in the processing of emotional information in healthy volunteers (Harmer *et al*. 2003*a*, *b*; Browning *et al*. 2007). Because this action could be relevant to the way in which antidepressant drugs produce their therapeutic effects it is important to find out whether other antidepressant treatment modalities also positively bias emotional processing. Preliminary evidence suggests that high-density negative ion (HDNI) treatment produces antidepressant effects in well-controlled small-scale studies of patients with winter depression in which it is as efficacious as bright-light treatment (Terman *et al*. 1998; also see Terman & Terman, 2006). In addition, high-density ions appear effective in the treatment of chronic depression (Goel *et al*. 2005) and also in improving mood in mildly depressed students even with acute exposure (Goel & Etwaroo, 2006). We therefore assessed the effect of a single session of HDNI treatment on models of emotional processing in healthy volunteers.

We studied 30 healthy participants (17 females, 13 males, aged between 18 and 28 years) who were screened to be free of current or previous Axis I psychiatric disorder on the Structured Clinical Interview for DSM-IV (SCID-IV). None of the participants were

currently taking medications or had previous experience of negative air ionization treatments. Participants were randomly assigned to a HDNI or control condition in a single-blind parallel-group design. HDNI treatment was delivered by a SphereOne FreshAIR Negative Ionizer (SphereOne Inc., USA) with wrist strap, shown to be effective in previous studies of winter depression. The device was deactivated for the control condition but this was not visible to participants. Participants received 30-min HDNI exposure and then began the emotional test battery described below. During this period, which lasted for about a further 60 min, the HDNI treatment was continued.

Subjective state before and at the end of the 30-min HDNI treatment period was measured by six visual analogue scales (VAS) designed to capture the following emotions: happiness, sadness, hostility, alertness, anxiety and calmness. Participants were also asked to guess which condition they thought they had received. The emotional test battery employed has been previously described (Harmer *et al*. 2003*a*, *b*; Browning *et al*. 2007) and consisted of an emotional categorization task with surprise emotional recall and recognition, a facial expression recognition test, and a dot-probe task of attention with masked and unmasked conditions.

The two treatment groups did not differ significantly on any the following baseline variables: age, gender, Beck Depression Inventory (BDI; Beck *et al*. 1961), trait scores on the Eysenck Personality Questionnaire (Eysenck & Eysenck, 1991), and verbal IQ measured by the National Adult Reading Test (NART; Nelson, 1982; data not shown). The majority of participants in both groups (77% overall) guessed that they were in the control condition and there were no effects of HDNI treatment on any of the VAS ratings (all p values >0.1). To examine mood response as a function of initial mood, correlations between BDI score at baseline (range 0–15) and mood response were computed for the six measures of subjective state in the group receiving HDNI treatment. This revealed a positive correlation between BDI score and increased calmness following the HDNI treatment ($r=0.5$, $p<0.05$), but not after sham treatment ($r=-0.1$, $p=0.7$), suggesting there may be some very subtle effects in those with low mood at the start of the study. None of the other correlations were statistically significant (all p values >0.08).

HDNI treatment did not change reaction times to categorize positive and negative self-descriptor words [positive: 955.49 ± 152.97 *v.* 998.94 ± 117.75 ms; negative: 994.16 ± 123.96 *v.* 1000.5 ± 162.57 ms; condition x emotion valence interaction: $F(1,26)=0.285$, $p=0.598$]. However, HDNI did alter emotional recall as judged by a significant emotion valence x condition interaction

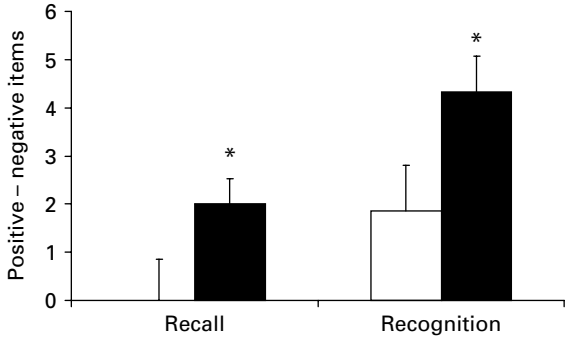

Fig. 1. Memory bias for positive *versus* negative information following negative ion treatment (■) or sham treatment (□). Values represent mean positive minus negative items recalled (left) or recognized (right) in the emotional memory task, ±S.E.M. Asterisks represent statistical significance of comparisons between groups (* $p<0.05$).

[$F(1,27)=4.073$, $p=0.05$] where, relative to controls, HDNI-treated participants recalled more positive and fewer negative words (Fig. 1). HDNI also influenced emotional word recognition shown by a significant emotion x condition interaction [$F(1,26)=5.057$, $p=0.047$] with the HDNI treatment resulting in participants recognizing fewer negative and more positive words (Fig. 1). In contrast to these effects on emotional recall and recognition, HDNI did not alter performance on the facial expression recognition or dot-probe tasks (data not shown).

Our findings indicate that HDNI treatment produces a positive bias in emotional recall and recognition. Participants were unable to reliably guess the condition that they were in, suggesting that the procedure was effective in limiting subject-expectancy bias in the results. These findings are similar to those we have obtained in healthy volunteers with the use of antidepressant medications such as citalopram (Harmer *et al*. 2003*a*), reboxetine (Harmer *et al*. 2003*b*) and mirtazapine (Arnone *et al*. 2009). Thus it is possible that early effects to produce positive biases in emotional memory might be a common property of treatments that possess efficacy in clinical depression. This is consistent with the key role that cognitive formulations of depression attach to negative memory biases in the maintenance of depressive states (e.g. Beck *et al*. 1979).

Conventional antidepressant drugs also produce evidence of positive emotional biases in attention and perception with single-dose administration (Harmer *et al*. 2003*a*, *b*; Browning *et al*. 2007); however, HDNI treatment did not influence these processes as judged by the facial expression recognition or dot-probe tasks. Further work will be needed to establish the clinical implications of this more restricted profile of action of HDNI treatment. For example, it may mean that HDNI

https://doi.org/10.1017/S0033291709990444 Published online by Cambridge University Press

has a rather weaker antidepressant effect than monoamine-potentiating agents. Alternatively it could suggest that the clinical efficacy of HDNI is restricted to depressive states, which are particularly associated with memory biases, and not extend into anxiety disorders which appear to be more dependent on early attentional and perceptual biases. Characterization of the effects of repeated treatment with HDNI is needed to evaluate this further.

Declaration of Interest

P. J. Cowen has served as a paid member of advisory boards for DSM, Eli Lilly, Lundbeck, Sevier, Wyeth, and Xytis. C. J. Harmer is on the advisory board of P1vital and has received consultancy fees from Servier, P1vital, Lundbeck, GSK, and Merck-Sharpe and Dohme. She holds shares in P1vital.

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https://doi.org/10.1017/S0033291709990444 Published online by Cambridge University Press