

BODY TEMPERATURE REGULATION AS A NOVEL ANTIDEPRESSANT STRATEGY



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BACKGROUND

- Current treatments for major depressive disorder (MDD) include medication, cognitive-behavioral therapy, and electroconvulsive therapy. While effective, these treatments are often complicated by delay in efficacy and adverse effects, indicating a need for novel therapies.
- Patients with MDD often demonstrate altered circadian rhythms and body temperature¹, providing another target for therapy. Whole-body hyperthermia (WBH) is an emerging strategy that has shown benefits for mood responses in recent studies.
- We report a review of studies in which WBH has been studied as a treatment for early and sustained mood responses for patients with MDD.

METHODS

- We performed a PubMed literature search using the terms “hyperthermia,” “major depressive disorder,” “whole-body hyperthermia,” and “hyperthermia psychiatric” to gather randomized controlled trials and uncontrolled studies in which human participants underwent hyperthermia protocols with mood assessment.
- Studies were published before December 2023 and were in any language.

RESULTS

- Eight studies met full criteria: Five randomized controlled trials and three uncontrolled studies.
- Five studies applied a single session of infrared radiation; two studies used multiple sessions of hyperthermic baths; one study used hot yoga.
- All studies reported improvement in self-reported depression symptoms. This improvement often started immediately after treatment. In some studies, this improvement lasted up to six weeks after completion of treatment (p<0.05).
- WBH improved depressive mood symptoms in subjects with diagnosed MDD and subjects without MDD.

SUMMARY OF RESULTS

Design, Intervention, N	Results	Reference
Non-controlled experiment: 1-hour exposure to radiative heat (41.8°C) under sedation. N=7 patients undergoing chemotherapy without psychiatric diagnosis.	Improved POMS score at 72 hours after treatment (p<0.05). Transient decrease in vigor (p<0.03) and transient increase in fatigue (p<0.02).	Koltyn et al., 1992 ²
Non-controlled experiment: 2-hour infrared WBH. N=16 patients with MDD.	Overall, WBH reduced CES-D symptoms five days after treatment (p<0.001). Three patients were taking medication and did not report improvements in mood as a result of WBH.	Hanusch et al., 2013 ³
RCT: 1 session of infrared WBH to reach core temperature of 38.5°C. N= 15 MDD patients received WBH, N=11 MDD patients received sham treatment with weak heating.	Reduced HDRS scores in the WBH group compared to the sham group up to 6 weeks after treatment (p<0.001 at 1 week; p=0.001 at 2 weeks; p=0.02 at 4 weeks; p=0.02 at 6 weeks).	Janssen et al., 2016 ⁴
RCT: 8 sessions over 2 weeks of hyperthermic baths at 40°C until subjective discomfort. N=17 MDD patients received bath, N=19 MDD patients received sham treatment with low-intensity green light at room temperature.	Reduced HAM-D scores in the bath group compared to the sham group after treatment (p=0.037). Mood improvements persisted after treatment but equalized between groups 4 weeks later (p=0.238).	Naumann et al., 2017 ⁵
RCT: 16 sessions across 8 weeks of hyperthermic baths at 40°C until subjective discomfort, or physical exercise control. N=22 MDD patients received bath, N=23 MDD patients performed exercise.	Reduced HAM-D scores in the bath group compared to the exercise group 2 weeks into treatment (p<0.001), but not significantly different at conclusion of treatment (p=0.084).	Naumann et al., 2020 ⁶
Non-controlled experiment: 1 session of infrared WBH to reach core temperature of 38.5°C. N=25 adults without psychiatric diagnosis.	Trending reduction in QIDS scores (p=0.054) and reduced negative affect PANAS scores (p=0.022) one week after treatment. No differences in PANAS positive affect (p=0.465), GAD-7 (p=0.617), WHO-5 (p=0.894).	Mason et al., 2021 ⁷
RCT: 1 session of infrared WBH to reach core temperature of 38.5°C. N=16 MDD patients received WBH, N=14 MDD patients received sham.	Immediate increase in serum levels of IL-6 in WBH group compared to sham group after treatment (p<0.001). IL-6 increase is correlated with reduced HDRS scores six weeks after treatment (p=0.011).	Flux et al., 2023 ⁸
RCT: 8 weeks of repeated hot yoga sessions. N=33 MDD patients underwent hot yoga, N=32 MDD patients were on waitlist control.	Reduced IDS scores compared to baseline in the hot yoga group compared to the control group after treatment (p<0.001). Trending association between more yoga classes attended and IDS scores after treatment (p=0.09).	Nyer et al., 2023 ⁹

DISCUSSION

- All studies showed improvements in mood after WBH treatment, some lasting six weeks after completion. While antidepressant medication often takes weeks for full effect, mood symptoms frequently improved immediately after treatment. Each study excluded subjects with a recent medication change, so more studies would be needed to evaluate WBH as a bridging therapy after starting a new medication.
- One study found an immediate increase in serum IL-6 level after WBH, which correlated with six-week symptom improvement despite normalization of IL-6. The role of IL-6 as an antidepressant continues to be elucidated.
- WBH was applied to patients who either were not taking medication or remained on a consistent dose. The identity of the medications was not revealed. The influence of concurrent medication as a factor in recovery was not analyzed. The relative effectiveness of combining WBH and medication has not been studied.
- Body temperature follows circadian rhythms, which are often disrupted in MDD. WBH may re-entrain rhythms in the thermoregulatory system as a component of symptom improvement.
- Common limitations: small sample sizes, subjects were taking no medication or consistent doses without recent changes, adults of various ages, variable WBH conditions and control conditions.
- Conclusion: WBH is a promising treatment for immediate and extended mood improvements for patients with MDD, but larger sample sizes with standardized protocols are needed.

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