

Imaging and menopausal hot flashes

Comment on: Farrell MJ. Regional brain responses in humans during body heating and cooling. *Temperature* 2016; 3:220-31; <http://dx.doi.org/10.1080/23328940.2016.1174794>

Farrell recently published an interesting review paper on imaging human brain responses during heating and cooling.¹ Here, he discussed our work on imaging such responses during menopausal hot flashes (HFs).²

Hot flashes are triggered by small elevations in core body temperature acting within a greatly reduced inter-threshold zone in symptomatic menopausal women.³ This reduction is due to estrogen withdrawal and increased sympathetic activation among other factors.⁴ There is an α_2 -adrenergic component in this mechanism, as demonstrated by the fact that HFs can be provoked by yohimbine, an α_2 -adrenergic antagonist and inhibited by clonidine, an α_2 -adrenergic agonist.⁵

We have demonstrated, in this temporal sequence, activation of specific areas of the brainstem, insula, and prefrontal cortex during HFs using fMRI.² The rise in brainstem activity occurred before HF onset, as detected by sternal skin conductance level, an electrical measure of sweating. Since this was the earliest measured activation, we suspect that it represents the HF trigger. Activity in the insula and prefrontal cortex trailed that in the brainstem.


Recently, we extended the temporal window of our analyses to examine functional connectivity of these areas using psychophysiological interaction analysis, a method also employed by Farrell and colleagues. Here, we found significantly increased modulation by the brainstem in the interval before the hot flash and even occurred. We observed this in the following a priori defined areas: the insula, the dorsal prefrontal cortex, the anterior cingulate cortex, and the basal ganglia. The physiological significance of these results is not presently known.

References

- [1] Farrell MJ. Regional brain responses in humans during body heating and cooling. *Temperature* 2016; 3:220-31; <http://dx.doi.org/10.1080/23328940.2016.1174794>
- [2] Diwadkar VA, Murphy ER, Freedman RR. Temporal sequencing of the brain activations during naturally occurring thermoregulatory events. *Cereb Cortex* 2014; 24:3006-13; PMID:23787950; <http://dx.doi.org/10.1093/cercor/bht155>
- [3] Freedman RR, Krell W. Reduced thermoregulatory null zone in postmenopausal women with hot flashes. *Am J Obstet Gynecol* 1999; 181:66-70; PMID:10411797; [http://dx.doi.org/10.1016/S0002-9378\(99\)70437-0](http://dx.doi.org/10.1016/S0002-9378(99)70437-0)
- [4] Freedman RR. Menopausal hot flashes: mechanisms, endocrinology, treatment. *J Steroid Biochem Mol Biol* 2014; 142:115-20. Review; PMID:24012626; <http://dx.doi.org/10.1016/j.jsbmb.2013.08.010>
- [5] Freedman RR, Woodward S, Sabharwal SC. Alpha₂-adrenergic mechanism in menopausal hot flashes. *Obstet Gynecol* 1990; 76:573-8; PMID:2170883

Robert R. Freedman

*Departments of Psychiatry & Behavioral Neurosciences and
Obstetrics and Gynecology Wayne State University
School of Medicine, Detroit, MI, USA*

 aa2613@wayne.edu