AMERICAN JOURNAL OF PHYSIOLOGY
ENDOCRINOLOGY AND METABOLISM

Am J Physiol Endocrinol Metab 320: E999–E1000, 2021.
First published April 12, 2021; doi:10.1152/ajpendo.00657.2020

POINT:COUNTERPOINT

Point: An alternative hypothesis for why exposure to static magnetic and electric fields treats type 2 diabetes

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Carter et al. (1) report that exposure to static magnetic and electric fields (sBE), for as little as 3 days, reverses glucose intolerance and insulin resistance in diet-induced and genetic mouse models of type 2 diabetes. They hypothesize that sBE triggers a systemic redox response to modulate insulin sensitivity and that sBE could therefore be used as a noninvasive treatment for type 2 diabetes. However, these authors were unable to define a mechanism to explain how sBE might alter reactive oxygen species (ROS) or to identify the specific proteins that mediate this effect. Given these limitations, we wish to propose an alternative hypothesis to explain their findings.

It is well established that the vestibular system in species ranging from humans to mice to zebrafish is impacted by static magnetic fields (2–4). This phenomenon is dependent on the magnetic field strength and is often manifested in humans as nystagmus (5). The static magnetic field used by Carter et al. (1) was ~100 times higher than the Earth's magnetic field, which is sufficient to induce these effects. The proposed mechanism for this effect on the vestibular system is thought to involve a Lorentz force resulting from the interaction of a strong static magnetic field with naturally occurring ionic currents flowing through the inner ear endolymph into vestibular hair cells (3). The resulting force within the endolymph is strong enough to displace the lateral semicircular canal cupula, inducing vertigo and horizontal nystagmus. Head motion in the magnetic field amplifies this effect.

When mice are exposed to sBE, movement in this magnetic field might cause disorientation and vertigo (3), whereas movement in the electrostatic field would be expected to put tension on mouse facial whiskers, which are exquisitely sensitive to motion. Therefore, sBE exposure would be expected to cause a temporary stress response leading to increased plasma catecholamine concentrations (6, 7). Although sBE-induced increases in circulating catecholamines would be expected to acutely promote glucose intolerance and insulin resistance due to increased white adipose tissue (WAT) lipolysis, increased hepatic glycogenolysis and gluconeogenesis, intermittent increases in plasma catecholamines would be expected to increase energy expenditure and promote AMP-activated protein kinase (AMPK) activation, which are both well established to reverse insulin resistance and hyperglycemia in high fat-fed mice and *db/db* mice. These effects would lead, in turn, to reductions in ectopic lipid content and more importantly reductions in plasma membrane associated *sn*-1,2-diacylglycerol content-nPKC activation in liver and muscle, reductions in liver glycogen content, increased glucose transport into muscle, increased liver and muscle fat oxidation, reduced hepatic de novo lipogenesis, and other related effects (7–10). In this regard, all insulin sensitivity measurements were performed when the mice were outside the sBE during which time they would have had time to acclimate to the absence of this sBE-induced stress response.

Consistent with this alternative hypothesis the authors report increased energy expenditure in their high fat diet (HFD)-fed mice exposed to sBE along with decreased body weight (Fig. S3D) and borderline statistically significant (P = 0.08) increases in heart rate (Table S1). Although they do not report the effect of sBE exposure on liver triglyceride content in their study, they do show histological changes (reduced vacuolization) in liver of sBE-exposed HFD-mice compared with the control HFD-mice (Fig. S3A), which would be consistent with sBE-induced reductions in hepatic triglyceride content in the HFD-fed mice. Moreover, sBE-exposed HFD-fed mice also displayed reduced RQ during the dark cycle, indicative of increased fat oxidation and consistent with increased AMPK activity (Fig. S3D).

This alternative intermittent stress hypothesis is readily testable by measuring plasma catecholamine concentrations with indwelling catheters, as well as urinary catecholamines, and additional measurements of heart rate, whereas mice are exposed to the sBE. In addition, liver and muscle triglyceride and glycogen content as well as AMPK activity in liver and skeletal muscle should be measured in all of their diet-induced and genetic mouse models of type 2 diabetes as well as uncoupling protein-1 (UCP-1) protein expression in brown adipose tissue, which would be predicted to be upregulated by intermittent increases in plasma catecholamines when the mice are put through the combined sBE exposure protocol (11).

Although the findings of Carter et al. (1) are intriguing, we believe it would be important to do these additional studies in rodents before performing similar studies in humans since if this alternative intermittent stress hypothesis is correct it will

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Submitted 8 March 2021 / Accepted 31 March 2021

demonstrate why sBE treatment would not translate as an effective therapy for type 2 diabetes in humans.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

K.F.P., D.L.R., and G.I.S. drafted manuscript; edited and revised manuscript; and approved final version of manuscript.

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