TRPV1, Nrf2, and COVID-19: Could Oxytocin Have a Beneficial Role to Play?

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Dear Editor,

Bousquet et al. [1] have elegantly and very informatively linked TRPV1, Nrf2, nutrients, and COVID-19: “rapid desensitization of TRAP1/TRPV1 by some ingredients in foods could reduce symptom severity and provide new therapeutic strategies.”

I would like to strengthen their links and proffer a peptide that could be important to their hypothesis: oxytocin.

Oxytocin is known for its function in labour and lactation and as the “love” hormone. However, it has numerous other actions and these actions provide additional supportive links and data. Oxytocin increases Nrf2 [2]. Oxytocin is a TRPV1 agonist and can desensitize the receptor [3]. Oxytocin also reduces TRPV1 activity indirectly via the vasopressin 1a receptor [4]. In addition, oxytocin can inhibit TRPV1 presynaptically [5]. In turn, thermal stimulation of TRPV1 can release oxytocin [6]. In terms of viral pathology, viruses can up-regulate TRPV1 [7], while down-regulating oxytocin receptors [8].

It is interesting to note that many of the “Nrf2-, TRPA1-, and TRPV1-interacting nutrients” (see Table 1 Bousquet et al. [1]) can also increase oxytocin or improve its function: *Lactobacillus* [9], quercetin [10], zinc [11], vitamin C [12], and vitamin D [13]. In another paper, Bousquet et al. [14] note that Nrf2-interacting nutrients also act on “mTOR, mammalian target of rapamycin;

PPAR γ , peroxisome proliferator-activated receptor; NF κ B, nuclear factor kappa B; ERK, extracellular signal-regulated kinases; and eIF2 α , elongation initiation factor 2 α .” Oxytocin also acts on these (in animal and in vitro studies): mTOR [15], PPAR γ [16], NF κ B [17], ERK [18], and eIF2 α [19]. Therefore, the endogenous neurohormone, oxytocin, is capable of both inhibiting TRPV1 and increasing Nrf2, and modulating numerous other pathways. This adds to the complexity of the link between TRPV1 and Nrf2.

This also raises some questions and gaps in knowledge. Does oxytocin act as part of a nutrient-oxytocin-Nrf2 pathway or does it act in parallel? In addition, can oxytocin act synergistically with these nutrients?

Not surprisingly, oxytocin has already been proposed as a treatment for COVID-19 due to numerous anti-inflammatory properties [16], antioxidant properties [20], anti-diabetic properties [21, 22], cardioprotective properties [23], and even possible direct antiviral properties [24]. It is safe and easily administered intranasally [25].

I hope these additional links will advance the understanding of how TRPV1, Nrf2, and nutrients interact, and therefore, strengthen Bousquet’s hypothesis and importantly, I hope this will lead to further research in this area and new therapeutic strategies.

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Author Contributions

Phuoc-Tan Diep contributed to conceptualization, methodology, and writing.

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