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## Could oxytocin reduce autoimmune disease in COVID-19?

### ARTICLE INFO

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### ABSTRACT

Disruption of immune and neuroendocrine system function has been shown to play a key role in COVID-19. Oxytocin is vitally important for the immune and neuroendocrine systems. However, oxytocin dysfunction might occur in COVID-19 leading to autoimmune disease. Intranasal oxytocin may be effective in turning off an overactive immune system. This could be a powerful approach to avoid possible autoimmune diseases after COVID-19.

### Dear editor

Jara et al. provided an excellent explanation of how the immune system and the neuroendocrine system function in regard to COVID-19 and autoimmunity [1]. However, we would like to highlight an overlooked part of the hypothalamic-pituitary axis: oxytocin. It is a neurohormone produced in the hypothalamus and secreted from the posterior pituitary gland and it is of vital importance to the immune and neuroendocrine systems [2]. Indeed, it has been shown that oxytocin can suppress the up-regulation of toll-like receptor 4 (TLR4) [3]; suppress the release of interleukin 6 (IL-6) [4,5], tumor necrosis factor alpha (TNF-alpha) [5]; inhibit the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway [6]; increase FOXP3+ regulatory T cells [7], modulate neutrophils [8], mast cells [9] and macrophages [10]. In other words, it may be able to turn off an activated proinflammatory immune system and therefore reduce the likelihood of autoimmune disease [11]. Last, but not least, oxytocin could be a direct antiviral against SARS-CoV-2 [12] thus limiting the initial infection and subsequent inflammation.

So, is it possible that SARS-CoV-2 infection disrupts oxytocin function? We believe so.

Jara et al. note that the hypothalamus can be infected by SARS-CoV-2 [1]. Oxytocin neurones in the hypothalamus most probably co-express angiotensin-converting enzyme 2 (ACE2) and transmembrane protease, serine 2 (TMPRSS2) and could therefore be infected [13]. Also, the pituitary gland is not isolated from the systemic circulation by the blood brain barrier [14] and therefore could be infected haematogenously. Thus central infection could lead to a reduction in oxytocin production. Peripherally, SARS-CoV-2 infection of the vagus nerve [15] may also lead to reduced oxytocin function [7]. In addition, Liu and Conboy also showed that the oxytocin receptor can be down-regulated by viral infections [16]. Further, reduced thymic function in severe COVID-19 [17,18], could result in reduced immune protection for the oxytocin peptide [19] and presumably lead to the production of oxytocin autoantibodies [20] as well as a general increase in autoimmunity. Also oxytocin function decreases with age [21].

It is, therefore, a distinct possibility that oxytocin dysfunction occurs

in COVID-19 and could lead to immune dysfunction and possibly to autoimmune disease. Unfortunately, to our knowledge, plasma levels of oxytocin have not been measured in COVID-19 patients. However, the oxytocin signaling pathway was reduced in the nasopharyngeal metabolome of such patients [22]. It would seem a natural step to use oxytocin to turn off, to deactivate, an over-active immune system. Intranasal oxytocin may be particularly effective as it may also stimulate endogenous release of oxytocin [23]. This may provide a powerful approach to head off autoimmune disease post COVID-19.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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