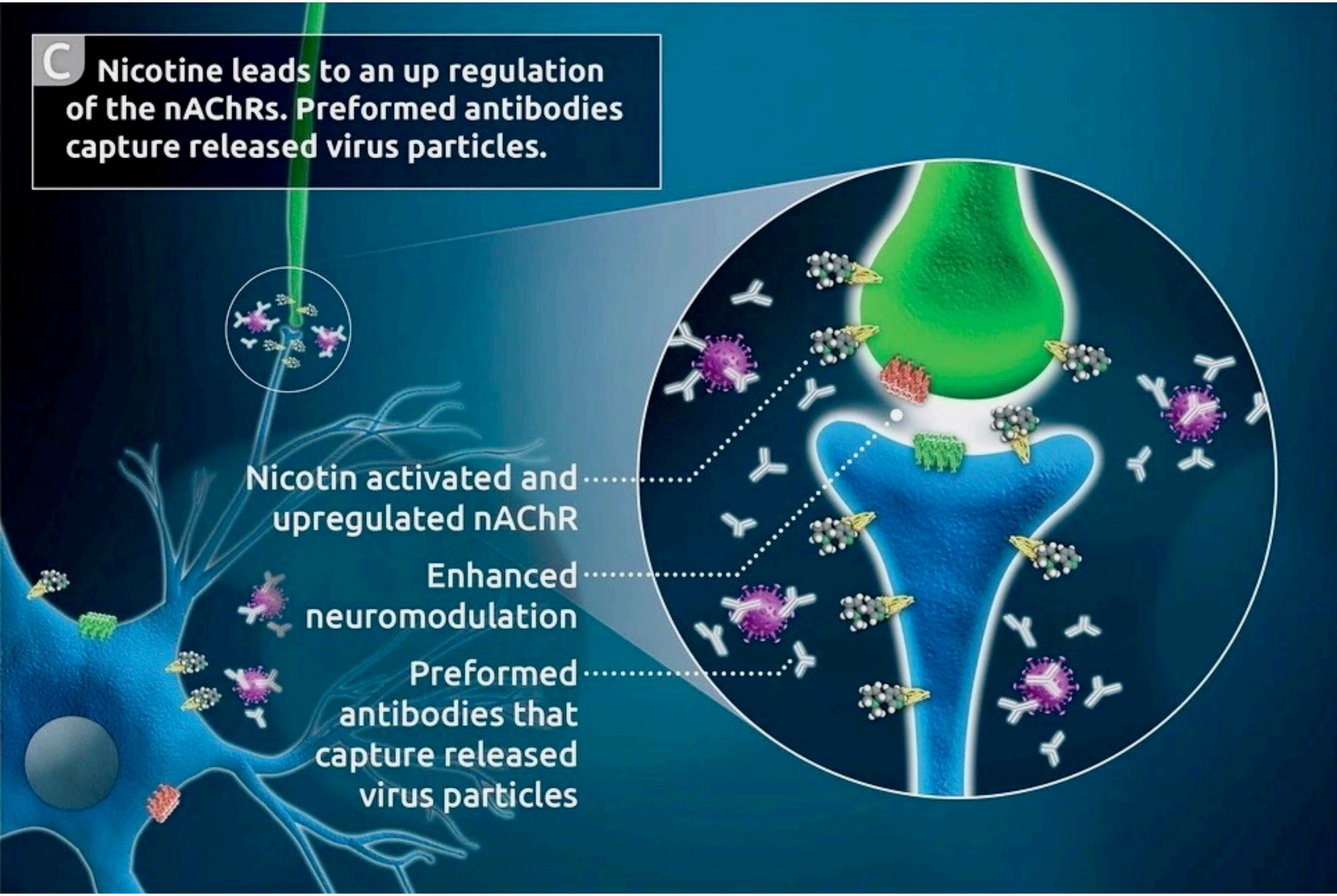
C Nicotine leads to an up regulation of the nAChRs. Preformed antibodies capture released virus particles.
Nicotin activated and upregulated nAChR
Enhanced neuromodulation
Preformed antibodies that capture released virus particles

COVID-19 – the ultimate nfκB rush

and the crucial importance of nicotinic acetylcholine receptors

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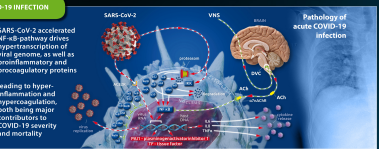
PATHOLOGY OF COVID-19 INFECTION



SARS-CoV-2 accelerated NF-κB pathway drives hypertranscription of viral genome, as well as proinflammatory and procoagulatory proteins

leading to hyper-inflammation and hypercoagulation, both baring major contributors to COVID-19 severity and mortality

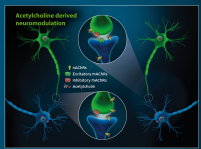
The SARS-CoV-2 virus replicates via vast acceleration of the transcriptional nfκB-pathway, thereby inducing unrestricted distribution of pro-inflammatory cytokines[1] and anti-fibrinolytic (PAI1) as well as procoagulatory (TF) coagulation factors[2]. This leads to cytokine storm with severe respiratory dysfunction (ARDS) and multi-organ failure (MOF) as well as micro- and macrovascular thrombotic occlusion with tissue hypoxemia and hemodynamic breakdown. The only physiologic mechanism capable to interrupt this vicious circle is the vagal-determined cholinergic anti-inflammatory pathway (ICAP)[3]. This is via acetylcholine (ACh) attachment to nicotinic acetylcholine receptors (nAChRs) followed by immediate interruption of nfκB-distribution. This makes individuals with unimpaired vagal signaling experience mild to moderate course of COVID-19. In contrast, depressed vagal function due to preexisting conditions can lead to severe COVID-19 cases and fatality.

Besides, ACE-2 receptor-derived cell entry viral spike glycoprotein (SPG) has been shown to attach to nAChRs in a non-intrinsic fashion[4]. This causes further compromised anti-inflammatory cholinergic action.

CHOLINERGIC NEUROMODULATION

Additionally, to the inflammation-restraining function nAChRs are present on almost every pre- and postsynaptic, as well as axonal and neuronal cell body membrane. Here they take responsibility for the regulation of neural excitability, as well as the amount and velocity of transmitter release into the synaptic cleft. This AChR-derived mechanism, adapting every neural signal to the requirements of the whole body is called neuromodulation[5]. It orchestrates network operations between several core groups and synchronizes response behavior to internal and external stimulation.

Thus, physiological functions like sleep, arousal, fatigue, anxiety, nutritional behavior, cognition, and central pain processing are interactively regulated by nAChR-derived cholinergic neuromodulation[5].

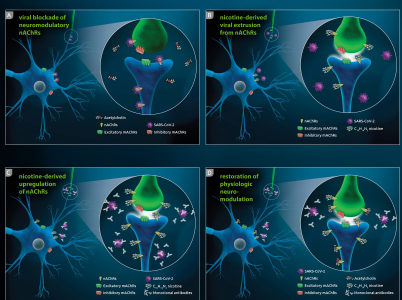


Cholinergic Neuromodulation

leads to:
- synchronized response behavior of different core groups to stimulation
- improved signal to noise ratio
- adaptive coordination of neuronal signaling

is involved in:
- synaptic plasticity
- neuronal development
- learning processes in general

regulates networking of functions such as:
arousal, sleep, fatigue, anxiety, nutritional behavior, cognition, central processing of pain[5]



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3 Tracey KJ. Physiology and immunology of the cholinergic antiinflammatory pathway. Journal of Clinical Investigation 2007; 117: 289–96.
4 Changeux JP, Amoura Z, Rey FA, Miyara M. A nicotinic hypothesis for Covid-19 with preventive and therapeutic implications. C R Biol. 2020 Jun 5;343(1):33–9.
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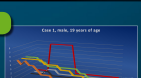
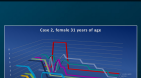
It is easy to imagine, that non-intrinsic blockade of neuromodulatory nAChR function is followed by a myriad of unspecific complaints like chronic fatigue, dizziness, low-grade fever, anosmia, memory lapses, agnosia, muscle weakness, diarrhea and bouts of vomiting, concentration and sleep difficulties, mood disorders, headache, cognitive impairment, motor deficits, new onset of diabetes and hypertension, dyspnea, and exercise intolerance.

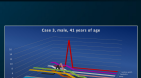
Thus, neuromodulation impairment explains the until recently undeciphered picture of long-haul COVID in a very plausible manner.

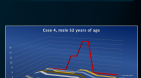
METHODS, MATERIAL AND RESULTS

We treated several non-smoking long-haul COVID patients with the use of a nicotine patch (7.5 mg/d). This resulted in immediate relief and prompt disappearance of all symptoms with no subsequent recurrence.









Post-COVID-19 syndrome is a severe disorder of cholinergic neurotransmission and responds to the application of nicotine.