Nicotine-Therapy

Various proteins of viral origin or from vaccination processes (e.g. the spike protein) are apparently able to block nicotinic acetylcholine receptors (nAChR). Fluoroquinolones have long been recognised as inhibitors of GABA-A receptors. A study from 2022 has now shown that they also have a clear affinity with significant inhibition of nicotinic acetylcholine receptors (nAChR). These receptors, especially the α4β2-nAChR, are widely distributed in the central nervous system.
The nAChR is the main structure of cholinergic neuromodulation and is responsible for the coordinated interaction of neuronal networks.

Non-intrinsic nAChR binding can significantly impair integrative interneuronal communication.This could also explain some cognitive, neuromuscular and mood impairments as well as the autonomic symptoms that FQAD patients, but also other patients with CFS/ME, postVacc and Long-Covid, complain about.
The agonist ligand nicotine has up to 30-fold higher affinity for nACHRs than acetylcholine (ACh) itself or any other agent.It is therefore possible that nicotine could displace the blocking agent from the nAChR approach and clear the way for undisturbed cholinergic signalling.
In the best case scenario, this would ensure long-term undisturbed function, i.e. some prominent peripheral, neurogenic and central nervous symptoms (such as fatigue, headaches, odour disorders, cognitive disorders, PEM, sleep disorders or even autonomic problems) could disappear permanently.

Please try Nicotine patches as a 4-8 week course:
Take the lowest possible patch dose (7-7,5 mg per 24 hours). Start with a quarter of the patch for 3 days. From the fourth day onwards, use half a patch for 4 weeks.If you're in Europe where you cannot get half patches, do not cut the patch in half or you can get an uncontrolled release of nicotine which you surely do not want. Instead, put tape on half (or 3/4) of it and use the rest. Half patches are available in the U.S.
You might experience a few side effects for 3-5 days until the immune system can catch up to it. Usually, though, you'll pass through this stage fine.
If you have not seen any improvement after 4 weeks,
please take Ambroxol 75 ret once a day for the first 10 days as an accompaniment and for detoxification.
Do not push too hard if you see improvement. Instead, go slowly and give your body time to heal. All sorts of compensating changes can occur in people who have been ill for a long time and they will take time to reverse.
It is very important to adhere strictly to the pacing during and after the therapy and not to go overboard. Otherwise relapses will inevitably occur!
Please take 1 x Ambroxol 3 x 30mg (or 75mg retard) daily for the first 10 days as a detox measure for the blocking agents like FQs, spikes, etc..

I need a detailed report on the entire course of treatment and the subsequent therapy results via email 4 weeks after treatment please!

ACS Chemical Neuroscience

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Stoichiometry-Selective Antagonism of α4β2 Nicotinic Acetylcholine Receptors by Fluoroquinolone Antibiotics

Victoria R. Sanders, Aaron Sweeney, Maya Topf, and Neil S. Millar*

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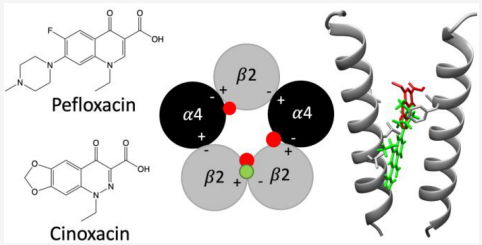
ABSTRACT: Quinolone antibiotics disrupt bacterial DNA synthesis by interacting with DNA gyrase and topoisomerase IV. However, in addition, they have been shown to act as inhibitors of pentameric ligand-gated ion channels such as $GABA_A$ receptors and the α7 nicotinic acetylcholine receptor (nAChR). In the present study, we have examined the effects of quinolone antibiotics on the human α4β2 nAChR, an important subtype that is widely expressed in the central nervous system. A key feature of α4β2 nAChRs is their ability to coassemble into two distinct stoichiometries, $(\alpha4)_2(\beta2)_3$ and $(\alpha4)_3(\beta2)_2$, which results in differing affinities for acetylcholine. The effects of nine quinolone antibiotics were examined on both stoichiometries of the α4β2 receptor by two-electrode voltage-clamp recording. All compounds exhibited significant inhibition of α4β2 nAChRs. However, all of the fluoroquinolone antibiotics examined (ciprofloxacin, enoxacin, enrofloxacin, difloxacin, norfloxacin, pefloxacin, and sparfloxacin) were significantly more potent inhibitors of $(\alpha4)_2(\beta2)_3$ nAChRs than of $(\alpha4)_3(\beta2)_2$ nAChRs. This stoichiometry-selective effect was most pronounced with pefloxacin, which inhibited $(\alpha4)_2(\beta2)_3$ nAChRs with an IC_{50} of 26.4 ± 3.4 μM but displayed no significant inhibition of $(\alpha4)_3(\beta2)_2$ nAChRs. In contrast, two nonfluorinated quinolone antibiotics (cinoxacin and oxolinic acid) exhibited no selectivity in their inhibition of the two stoichiometries of α4β2. Computational docking studies suggest that pefloxacin interacts selectively with an allosteric transmembrane site at the β2(+)/β2(−) subunit interface, which is consistent with its selective inhibition of $(\alpha4)_2(\beta2)_3$. These findings concerning the antagonist effects of fluoroquinolones provide further evidence that differences in the subunit stoichiometry of heteromeric nAChRs can result in substantial differences in pharmacological properties.



KEYWORDS: *Nicotinic acetylcholine receptor, subunit stoichiometry, antagonist, quinolone, antibiotic, pefloxacin*

INTRODUCTION

Nicotinic acetylcholine receptors (nAChRs) form part of the superfamily of pentameric ligand-gated ion channels, which includes receptors for 5-hydroxytryptamine (5-HT), γ-amino-butyric acid (GABA), and glycine.[1] Seventeen nAChR subunits have been identified in vertebrates (α1−α10, β1−β4, γ, δ, and ε) that can coassemble in a variety of combinations to generate a diverse family of pharmacologically distinct nAChR subtypes, including both heteromeric subunit combinations (such as α4β2) and homomeric complexes (such as α7).[2] Further complexity can arise as a consequence of nAChR subunits coassembling with different stoichiometries. For example, the α4 and β2 subunits can coassemble into pentameric complexes containing either two α4 and three β2 subunits ($(\alpha4)_2(\beta2)_3$) or three α4 and two β2 subunits ($(\alpha4)_3(\beta2)_2$).[3] As has been reported previously, the two stoichiometries of α4β2 nAChR differ in their sensitivity to acetylcholine (ACh) and, as a consequence, are often referred to as "high-sensitivity" and "low-sensitivity" subtypes, respectively.[4] Receptors containing α4 and β2 subunits mediate the effects of nicotine associated with tobacco smoking and are the site of action of drugs used to assist with smoking cessation.[5] In addition, α4β2 nAChRs are targets for drug discovery in areas such as cognition, attention, and pain.[6−8] In recent years, considerable attention has focused on studies of allosteric modulators of nAChRs that are thought to bind within the receptor's transmembrane domain.[9,10]

Quinolone antibiotics interact with two distinct targets within bacterial cells, DNA gyrase (DNAG) and topoisomerase IV, both of which are involved in bacterial DNA synthesis.[11] Quinolones inhibit DNA synthesis by stabilizing complexes of DNA and topoisomerase IV or DNAG which blocks the progression of the replication fork.[11] However, previous

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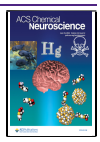

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HYPOTHESIS Open Access

Is the post-COVID-19 syndrome a severe impairment of acetylcholine-orchestrated neuromodulation that responds to nicotine administration?

Marco Leitzke*

Abstract

Following a SARS-CoV-2 infection, many individuals suffer from post-COVID-19 syndrome. It makes them unable to proceed with common everyday activities due to weakness, memory lapses, pain, dyspnea and other unspecific physical complaints. Several investigators could demonstrate that the SARS-CoV-2 related spike glycoprotein (SGP) attaches not only to ACE-2 receptors but also shows DNA sections highly affine to nicotinic acetylcholine receptors (nAChRs). The nAChR is the principal structure of cholinergic neuromodulation and is responsible for coordinated neuronal network interaction. Non-intrinsic viral nAChR attachment compromises integrative interneuronal communication substantially. This explains the cognitive, neuromuscular and mood impairment, as well as the vegetative symptoms, characterizing post-COVID-19 syndrome. The agonist ligand nicotine shows an up to 30-fold higher affinity to nAChRs than acetylcholine (ACh). We therefore hypothesize that this molecule could displace the virus from nAChR attachment and pave the way for unimpaired cholinergic signal transmission. Treating several individuals suffering from post-COVID-19 syndrome with a nicotine patch application, we witnessed improvements ranging from immediate and substantial to complete remission in a matter of days.

Keywords Post COVID 19 syndrome, Cholinergic neuromodulation, Nicotine, Nicotinic acetylcholine receptors, Vagus nerve signaling

Introduction

Post-COVID-19-syndrome

The coronavirus SARS-CoV-2 evoked pandemic calamity and took a toll on the world's population, with a death toll of 6 million victims within 30 months (COVID-19 Excess Mortality Collaborators 2022). Unprecedented scientific efforts led to a better understanding of the viral structure, transmission pathways and pathologic patterns, which ultimately helped to create sufficiently protective vaccines. The pathogen, however, always seems to be one step ahead; genetic variants of SARS-CoV-2 (Weisblum et al. 2020; Tang et al. 2021; Harvey et al. 2021; Mohiuddin and Kasahara 2022; Vaughan 2021; Karim and Karim 2021) present higher contagiousness (Karim and Karim 2021), compromise the sufficiency of vaccines (Harvey et al. 2021), promote escape from natural immunity (Harvey et al. 2021; Karim and Karim 2021) or reveal new pathology patterns (Abdelnabi et al. 2021).

Meanwhile, we are becoming more and more aware that even after convalescence from acute COVID-19, the suffering in many cases is not yet over (Rimmer and Covid-19, 2020). Symptoms such as chronic fatigue

*Correspondence:
Marco Leitzke
marco.leitzke@gmx.de
Department of Anesthesiology, Helios Clinics, Colditzer Straße 48, 04703 Leisnig, Germany