Nicotine action on neuronal networks of the prefrontal cortex: targets for cognitive enhancement in neuropsychiatric disorders

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Title of project or programme

Title of PI	Nicotine action on neuronal networks of the prefrontal cortex: targets for cognitive enhancement in neuropsychiatric disorders

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
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- Netherlands

Source of funding information

Netherlands Organisation for Health Research and Development (ZonMw)

Total sum awarded (Euro)

600000

Start date of award

15-12-2006

Total duration of award in months

60

The project/programme is most relevant to

- Neurodegenerative disease in general

Keywords

Nicotine, Alzheimer’s disease, Parkinson’s disease, schizophrenia and ADHD, neuronal and synaptic

mechanisms

Research abstract in English

Nicotine has been shown to improve cognitive function in humans. Nicotinic treatments are being developed as therapy for cognitive dysfunction in patients suffering from neuropsychiatric disorders such as Alzheimer’s disease, Parkinson’s disease, schizophrenia and ADHD. Critical for development of nicotinic therapeutics is an understanding of neuronal and synaptic mechanisms underlying nicotinic involvement in cognitive function. Nicotinic agonists act beneficial on several aspects of cognition including working memory, attention, learning and memory. Different brain areas and different nicotinic receptors are involved in these effects. Little is known of how nicotine enhances attention function and we understand little of the cellular and synaptic mechanisms involved. With the research proposed here, I aim to resolve which nicotinic receptor subtypes are involved in improving attention function and understand neuronal and synaptic mechanisms underlying this cognition enhancement in prefrontal cortex (PFC), which is involved in attention.
Nicotine also improves cognitive performance in primates and rodents. I will study short- and long-term effects mediated by different nicotinic receptor types on synaptic and cellular properties of neuronal networks in mouse PFC, using a combination of two-photon imaging and electrophysiology in living brain slices. To assess roles of distinct receptor types in modulating PFC circuitry and attention behaviour I will use transgenic mice with genetically altered functionality of specific nicotinic receptor subunits. I will study how nicotinic modulation of neuronal and synaptic activity is affected when a specific receptor subunit is lacking. By re-expression of specific subunits selectively in PFC of knock out mice lacking that particular subunit with lentiviral vectors, I will examine whether nicotinic modulation of neuronal networks and behavioural attention performance is restored. This research will increase our understanding of how nicotine acts as cognitive enhancer and identify specific nicotinic receptors as target for therapeutic treatments of patients suffering from cognitive dysfunction.

Lay Summary
In which category does this research fall?

- Basic research