

# The association between tobacco smoking and brain alterations in schizophrenia:

## A systematic review of magnetic resonance imaging studies

M. Koster<sup>1</sup>, L. Mannsdörfer<sup>1</sup>, M. van der Pluijm<sup>1</sup>, L. de Haan<sup>1</sup>, T. Ziermans<sup>2</sup>, G. van Wingen<sup>1</sup>, J. M. Vermeulen<sup>1</sup>.

<sup>1</sup>Amsterdam UMC, Psychiatry, Amsterdam, the Netherlands. <sup>2</sup>Universiteit van Amsterdam, Psychology, Amsterdam, the Netherlands.

m.koster5@amsterdamumc.nl

### Background

Tobacco smoking amongst patients with schizophrenia is 3 times higher compared to the general population [1] and associated with worse clinical outcomes such as readmission [2]

Neuroimaging research can uncover shared neurobiological mechanisms and consequences in patients, aiding development of pharmacological/health interventions to improve clinical outcomes and life expectancy of patients

### Aim

Create comprehensive understanding of the potential neurobiological consequences of chronic tobacco smoking in schizophrenia

### Results



**8 structural studies** show independent and additive grey matter reductions in PFC, insula, ACC, PCC, hippocampus, and amygdala in relation to smoking and SSD



**8 resting-state studies** mainly suggest an association between smoking and improvements in connectivity deficits linked to SSD, but 2 studies suggest an additive negative effect. Overall, smoking appears associated with distinct effects on neural dynamics in individuals with and without SSD



**6 task-based studies** point to distinct neural activation patterns in SSD smokers, with increased reward system sensitivity, and disrupted neural pathways that mediate cognitive and affective processing of the negative consequences of smoking

### Discussion

SSD-related neurobiological alterations at nACh receptor level may explain differential effects of nicotine on the psychotic versus non-psychotic brain (Figure 1)

Most resting-state (63%) and task-based (50%) studies employed data from the same samples. The interdependence of results could mistakenly enhance significance of findings, or limit the generalizability

95% of studies were cross-sectional, preventing establishing temporal relationships or causality

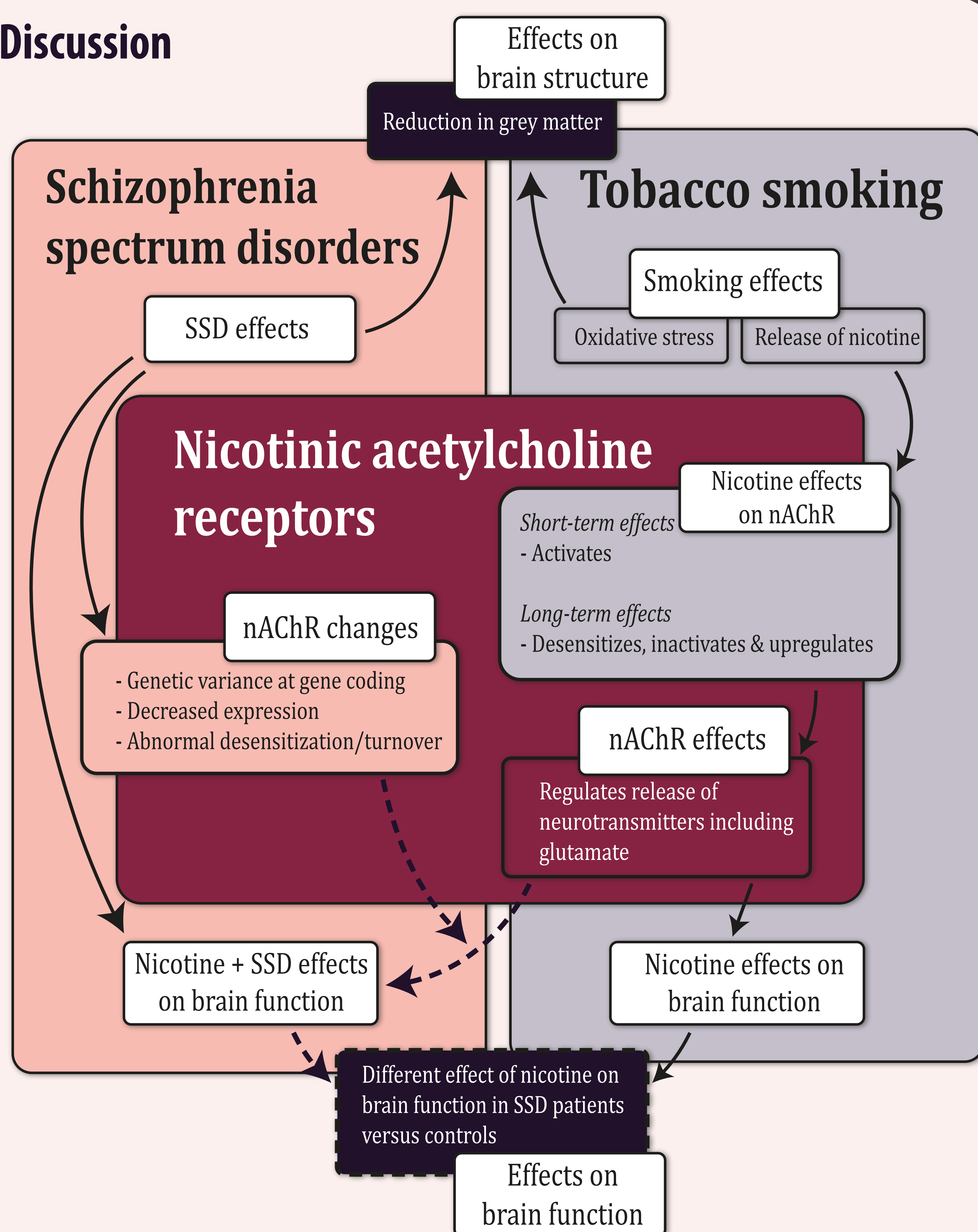
### Future directions

Future endeavors include longitudinal studies to distinguish pre-existing anatomical and physiological differences from the (long-term) effects of smoking, and investigating nAChR (dys)functioning, e.g. using positron emission tomography

### Methods

Inclusion criteria were; 1) Studies in patients with a schizophrenia spectrum disorder (SSD), 2) investigating current habitual cigarette smoking SSD patients versus non-smoking SSD patients, or smoking or non-smoking controls, 3) using structural, functional, neurochemical magnetic resonance imaging (MRI)

### Discussion



**Figure 1 Theoretical framework presenting the hypothesized relationship between chronic tobacco smoking, brain structure, and brain function in patients with SSD.** Dashed arrows/boxes indicate hypothesized effects. Structural studies show that smoking has a negative effects on grey matter, potentially worsening SSD-related abnormalities. Functional findings show that smoking appears associated with distinct effects on neural dynamics in patients versus controls, posing a possible schizophrenia-specific neurobiology of tobacco addiction. In SSD, a central role of nicotinic acetylcholine receptors (nAChRs) is hypothesized, with genetic variations [3] and expression changes [4] which in turn could affect neurotransmitter release and thus the brain's response to nicotine, diverging from controls.

### References

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