

The Neurobiological Pathway Towards Suicidal Ideation – Cerebrospinal Fluid Markers, Cognitive Impairment and Brain Imaging

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i hörsal Arvid Carlsson, Akademikum, Medicinaregatan, Göteborg, den 1 september 2025, klockan 13.00

av Irma Rymo

Fakultetsopponent:

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Avhandlingen baseras på följande delarbeten

- I. Rymo, I., Kern, S., Bjerke, M., Zetterberg, H., Marlow, T., Blennow, K., Gudmundsson, P., Skoog, I., Waern, M. (2017): CSF YKL-40 and GAP-43 are related to suicidal ideation in older women. *Acta Psychiatr Scand.* 135: 121–133.
- II. Rymo, I., Fässberg, MM., Kern, S., Zetterberg, H., Skoog, I., Waern, M., Sacuiu, S. (2023): Mild cognitive impairment is associated with passive suicidal ideation in older adults: A population-based study. *Acta Psychiatr Scand.* 148: 91–101.
- III. Rymo, I., Zetterberg, H., Blennow, K., Kern, S., Skoog, I., Sacuiu, S., Waern, M. (2025): High CSF neurogranin level is related to lifetime reports of passive suicidal ideation in a population-based sample of older adults. *J Psychiatr Res.* 181: 340–347.
- IV. Rymo, I., Zetterberg, H., Westman, E., Skoog, I., Waern, M., Sacuiu, S. Brain morphology and suicidal ideation: A population-based MRI study. *Submitterad.*

**SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR NEUROVETENSKAP OCH
FYSIOLOGI**



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Abstract

Suicidal behavior represents a complex, multifactorial phenomenon and remains a significant public health challenge. This thesis explores neurobiological and cognitive correlates of suicidal ideation in older adults, using biomarkers in cerebrospinal fluid (CSF), neuropsychiatric examinations, and magnetic resonance imaging (MRI). Drawing on four studies, the aim was to increase understanding of underlying mechanisms by investigating associations between glial activity, synaptic dysfunction, brain structure, cognitive impairment, and suicidal ideation using population-based samples.

In Paper I, higher CSF levels of YKL-40 and GAP-43, markers of glial activation and synaptic remodelling, were associated with recent suicidal ideation in older women, independent of depression status. Study II demonstrated an association between mild cognitive impairment (MCI) and both past year reports of life-weariness and death wishes in models adjusted for covariates including depression. MCI was also related to lifetime experiences of life-weariness. Study III found that individuals with high CSF neurogranin (Ng) level more frequently reported lifetime experiences of life-weariness, death wishes, and suicidal thoughts. The association between high CSF Ng level and lifetime suicidal ideation (all severity levels) remained significant in models adjusted for biomarkers related to Alzheimer's disease. Paper IV examined white matter lesions (WML) volume and grey matter volumes of the amygdala, hippocampus, and parahippocampus in relation to suicidal ideation. While no significant relationships were found for the grey matter regions, individuals who had seriously contemplated suicide exhibited greater WML volume, suggesting a potential contribution of white matter integrity to more severe forms of suicidal ideation.

Together, the findings contribute to a growing body of evidence supporting the role of neurobiological mechanisms in understanding suicidal behavior in aging populations.

Keywords: suicidal ideation, synaptic dysfunction, mild cognitive impairment

ISBN 978-91-8115-274-6 (TRYCK)

ISBN 978-91-8115-275-3 (PDF)