**Multi-air pollutant exposure and amyotrophic lateral sclerosis (ALS) diagnosis in Denmark**

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Amyotrophic lateral sclerosis (ALS) is a devastating and fatal neurodegenerative disease, with approximately half of patients dying within three years of symptom onset. Its aetiology remains elusive and known inherited mutated genes only account for 5–10% of the cases. There is some limited evidence to suggest ALS onset is associated with exposure to air pollution, and specifically to traffic-related pollution. However, previous smaller studies have only examined the association with relevant pollutants in separate models.

In the present study, we used prospectively collected data from the Danish National Registers system from 2,188 ALS cases diagnosed between 1989 – 2013 and matched on age, sex, and vital status to 6,766 controls. We used predictions from a validated spatio-temporal model to assign 5-year average exposures prior to diagnosis to nitrogen oxides (NOx), carbon monoxide (CO), elemental carbon (EC), fine particles (PM2*.*5), and ozone at residential addresses of study participants. We used a Bayesian hierarchical conditional logistic model to assess whether exposure to traffic- and non-traffic-related pollution is associated with ALS diagnosis, adjusting for potential confounders.

We found that for an inter-quartile range (IQR) increase in 5-year average concentrations, the joint effect of included traffic-related pollutants (NOx, CO, EC) was associated with an increase in odds of ALS diagnosis (8.4%; 95% credible interval [CrI]:-1.4, 18.9%). Increases in non-traffic related pollution resulted in an increase in odds for ozone (IQR=7.9 µg/m3) (6.6%; 95%CrI: -8.5%, 21.9%), and a decrease for PM2*.*5 (IQR=4.0 µg/m3) (-13.1%; 95%CrI: -35.8%, 10.7%). Overall, there was a 95% posterior probability of a positive association between the joint effect of included traffic-related pollutants and ALS diagnosis.

Our results indicate a potential positive association between ALS diagnosis and traffic-related pollution. Further work is needed to understand the role of air pollution on ALS pathogenesis and timing of onset.