LATE-BREAKING ABSTRACT: NO_2 and lung function: Mediation by DNA methylation

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Abstract

Background: Ambient levels of NO_2 exposure are consistently associated with a higher risk for respiratory exacerbations and lower lung function, but the mechanisms underlying this association are not clear. Possibly, differential DNA methylation associated with NO_2 exposure may play a mediating role in this.

Aim: Assess whether differential DNA methylation mediates the effect of NO_2 exposure on lung function.

Methods: 1017 subjects of the LifeLines cohort study, a large general population based cohort in the north of the Netherlands, were included. Blood-DNA methylation expressed as β-value was assessed using Illumina Methylation 450K chips. Outdoor annual mean concentration of NO_2 at the participant's home address was estimated using Land Use Regression (LUR) models.

Results: A 10 $\mu g/m^3$ increase in NO_2 concentration was marginally associated with higher levels of FEV_1/FVC (B=1.483, p=0.055). No significant association between NO_2 and FEV_1, FVC and FEF_{25-75} was found. Adjusted robust linear regression models, assessing 430,950 CpG probes, revealed significant associations between NO_2 exposure and 8 CpGs sites (Bonferroni corrected threshold: $p < 1.16E-7$) mapping to 8 genes. Two of these CpGs sites were also strongly and positively associated with FEV_1/FVC, but no mediation effect was seen (assessed with the Sobel test).

Conclusion: Although no mediation effect was found, NO_2 exposure was associated with differential methylation in CpGs that were positively associated with lung function. Since the level of NO_2 exposure in LifeLines is very low, replication of these findings is needed in other cohort studies with a broader range of exposure.