

Living in the city centre is associated with type 1 sensitization to outdoor allergens in Leipzig, Germany

Sensitization to type 1 allergens with clinical manifestation of allergic rhinitis (AR) and/or allergic asthma has been associated with several host and environmental factors. It was shown that the prevalence of AR is lower among people born and raised on a farm^{1,2} and different prevalence rates of type 1 sensitization between inner-city areas and suburbs as well as a clear urban-rural gradient with relevant early life factors for AR were reported from Northern Europe, with highest prevalence rates in subjects brought up in inner-city areas and lowest rates in those brought up in a farm with livestock.¹ A protective effect of early life endotoxin exposure was discussed to contribute to these regional differences.¹ In adults living close to a major road, an increased allergic sensitization to pollen was found.³

We aimed to cross-sectionally determine any differences in type 1 sensitization to inhalant allergens between subjects living in the city centre of Leipzig and those living in any of the outer boroughs. In parallel to recent reports on comorbidities in atopic diseases^{4,5} our second aim was to investigate any atopic and/or nonatopic comorbidities in subjects with type 1 sensitization.

The city of Leipzig, with 590 000 inhabitants, comprises an area of about 300 km². The city centre is characterized by several major roads, covers about 14 km², is divided into seven central boroughs, and had about 62 182 inhabitants in 2016.

Within the population-based LIFE-Adult-Study (Leipzig Research Centre for Civilization Diseases; trial period 8/2011-11/2014), an age- and gender-stratified random sample of 10 000 residents (age range 18-79 years) had undergone medical examinations (including skin prick test/SPT to six inhalant allergens: birch, timothy grass, mugwort, ragweed, alternaria, ALK-Abello, Hamburg, Germany) and answered interviews as well as questionnaires.

We compared subjects with positive (≥ 1 allergen) and negative SPT with regard to age, sex, body mass index (BMI), socioeconomic state (SES), place of residence, history of physician diagnosed AR, asthma, atopic dermatitis, autoimmune, rheumatic, inflammatory bowel or coronary artery disease, current smoking and stroke. Continuous variables were expressed as median and range, categorical variables as absolute or relative frequencies. For group comparisons, the Mann-Whitney *U* test was used for continuous variables and the chi-squared or Fisher's exact test for categorical data.

Multivariate binary logistic regression models adjusted for sex, age, SES, BMI and current smoking were used to investigate the associations of SPT results with comorbidities and associations of atopic diseases and those living in the city centre.

Out of the 10 000 study participants, 6047 underwent SPT (48% female, median age 52 years); 1608 (26.5%) were SPT positive; sensitization rates: birch 16.2% timothy grass 14.8%, mugwort 9.7%, ragweed 4.0% and alternaria 4.2%.

Subjects living in the city centre had more frequently positive SPT than those of the other boroughs (univariate OR = 1.5 with 95% CI [1.06; 1.69]; $P < .001$). Outdoor allergens investigated included typical seasonal allergens having shown highest sensitization rates in the German Health Study⁷. Also after adjusting for age, sex, BMI, current smoking and SES, positive SPT was significantly associated with living in the city centre (OR = 1.4 with 95% CI [1.1; 1.6]; $P = .002$).

With regard to other comorbidities, we could not confirm any independent association of type 1 sensitization with the nonatopic diseases investigated (Table 1), which is in contrast to what has been reported for atopic dermatitis.⁵

In conclusion, living in the city centre was shown to be associated with type 1 sensitization to inhalant outdoor allergens. As pollen collected along high-traffic roads were shown to have a higher allergenicity than pollen sampled in vegetated areas,^{8,9} one might speculate about traffic-associated pollution (TRAP) promoting type 1 sensitization.^{3,10} For the years 2005-2016, mean values for NO₂ were shown to be more than twice as high in the inner-city region (40-50 µg/m³) compared with outer city areas (about 20 µg/m³; <https://www.leipzig.de/>). A strong positive association between the distance to the nearest main road and asthma/hay fever and sensitization was already reported in children of the GINI/LISA study in Germany.¹⁰ A WHO's review concluded that substantial evidence indicates that TRAP can increase the risk of allergy development and exacerbate allergic reaction (<https://www.euro.who.int/>).

In summary, we observed increased sensitization rates to inhalant outdoor allergens in subjects living in the city centre of Leipzig. The factors contributing to these increased sensitization rates are not well understood but might be related to TRAP.

TABLE 1 Comparison of subjects with positive and negative skin prick test results with regard to baseline characteristics as well as atopic and nonatopic comorbidities

Factors	Patient characteristics			Result of multivariate analysis		
	SPT positive N = 1608	SPT negative N = 4439	P value	Odds ratio	P value	95% CI
Age median (range) in years	52 (19;79)	53 (19;80)	<.001	0.98	<.001	0.97; 0.98
Sex—female	774 (48.1%)	2349 (52.9%)	.001	0.74	<.001	0.64; 0.86
Overweight ≥ 25 kg/m ²	935 (59.9%)	2809 (64.6%)	.001	1.04	.623	0.89; 1.22
Current smoker	333 (21.3%)	969 (22.7%)	.241	0.97	.436	0.88; 1.05
SES low	257 (16.0%)	907 (20.5%)		-	-	-
SES middle	995 (62.1%)	2647 (59.7%)		0.85*	.103	0.69; 1.03
SES high	350 (21.8%)	877 (19.8%)	<.001	1.05**	.592	0.87; 1.26
Myocardial infarction	20 (1.3%)	96 (2.2%)	.021	0.67	.282	0.32; 1.40
Inflammatory bowel disease	14 (0.9%)	37 (0.8%)	.871	1.10	.827	0.46; 2.64
Coronary artery disease	29 (1.9%)	130 (3.0%)	.015	0.57	.082	0.31; 1.07
Stroke	19 (1.2%)	100 (2.3%)	.008	0.74	.360	0.38; 1.42
Autoimmune disease	47 (3.0%)	124 (2.9%)	.0766	0.68	.122	0.41; 1.11
Rheumatic disease	51 (3.3%)	199 (4.6%)	.025	0.91	.631	0.61; 1.35
Atopic dermatitis	95 (6.1%)	131 (3.0%)	<.001	1.20	.331	0.83; 1.75
Asthma	192 (12.3%)	156 (3.6%)	<.001	2.46	<.001	1.81; 3.34
Allergic rhinitis	668 (42.7%)	68 (1.6%)	<.001	47.85	<.001	35.97; 63.65

Abbreviation: SES—socioeconomic state

* low vs. middle; ** middle vs. high.

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CONFLICT OF INTEREST

There are no conflicts of interest.

AUTHOR CONTRIBUTIONS

Designed the study: Treudler, Simon, Loeffler

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