Impact of particulate matter of diameter inferior to 2,5 micrometer exposure on multiple sclerosis relapse

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Introduction :

Ambient air pollution, and notably particulate matter exposure has emerged as a global major health concern, leading to premature death of 3,1 millions of people worldwide(1), PM is subdivided according to size into coarse (PM10, diameter <10µm), fine (PM2.5, diameter <2.5µm), and ultrafine (PM0.1, diameter <0.1µm). Unlike PM10, PM2.5 mostly arise from combustion (Diesel exhaust), and are essentially composed by organic and elementary carbon, sulfate, nitrate and metals. PM2.5 can reach small alveoli, and ultrafine particles (PM0,1) have the ability to reach plasmatic circulation, and may penetrate central nervous system crossing hematoencephalic barrier(2) and through olfactory bulb(3). Exposure to PM exhibit systemic and cerebral inflammation, possibly through lymphocyte priming in the lung(4) and increase cerebral oxidative stress(5).

Various study have already highlighted an increase of relapse risk in multiple sclerosis affected patients exposed to PM of diameter inferior to 10 µm (PM10)(6-8). PM10 exposure is also associated with breakdown of hematoencephalic barrier demonstrated by gadolinium enhancement at cerebral MRI(9). However, to our knowledge, the effect of exposition to PM2.5 on multiple sclerosis relapse has never been assessed.

We conduced this study to determine the specific effect of PM2.5 on multiple sclerosis relapse.

Material and methods:

Area: Paris and Ile de France, France
Period: from first January 2009 to 31 December 2013.
Hospitalizations included using the French hospital administrative database: "Programme de Médicalisation des Sytèmes d'Information (PMSI)".

Inclusion criteria:
- Hospitalization in day hospital for multiple sclerosis relapse
- Patient personal address located in Ile de France
- day-hospital stay for 3 to 6 days

Pollution data was based on the high spatial resolution CHIMERE air quality model. Meteorological parameters were obtained from the French meteorological service Meteo France. Data on influenza like infection were obtained from the Sentinel Network. Pollen data were obtained from the Réseau National de Surveillance Aérobiologique (RNSA).

Statistical analysis: Case control study, each patient was his own control.

PM2.5 exposure was assessed by week before hospitalization, week [0] corresponding to the seven days ended by the hospitalization admission date.

The natural logarithm (Ln) of the average weekly PM2.5 exposure for each of the six weeks (week [0] to week [-5]) preceding hospitalization were compared to exposure during previous week (for example, LnPM2.5 exposure at week [0] was compared to LnPM2.5 exposure at week [-1], LnPM2.5 exposure at week [-1] was compared to LnPM2.5 exposure at week [-2]…), using a conditional logistic regression, adjusted on average weekly temperature, flu like syndrome rate, pollen exposure, and holiday period.
Successively, we evaluated the influence of age on the association between PM2.5 and relapse.

Results:

Table 1: Characteristic of included hospitalizations

Total of hospitalizations	**2109**
Age of patient, year, median (P25;P75)	40 (33;49)
Female, Number (Percentage)	1496 (70.93)
Department of the place of life, N (%)	
Paris	664 (31.48)
Seine Saint Denis	296 (14.04)
Hauts de Seine	286 (13.56)
Val d'Oise	217 (10.29)
Essonne	321 (11.15)
Val de Marne	173 (8.20)
Seine et Marne	160 (7.59)
Yvelines	84 (3.98)
Hospitalization duration, median (P25;P75)	3 (3;3)

Figure 1: address of living places of included patients in Ile de France

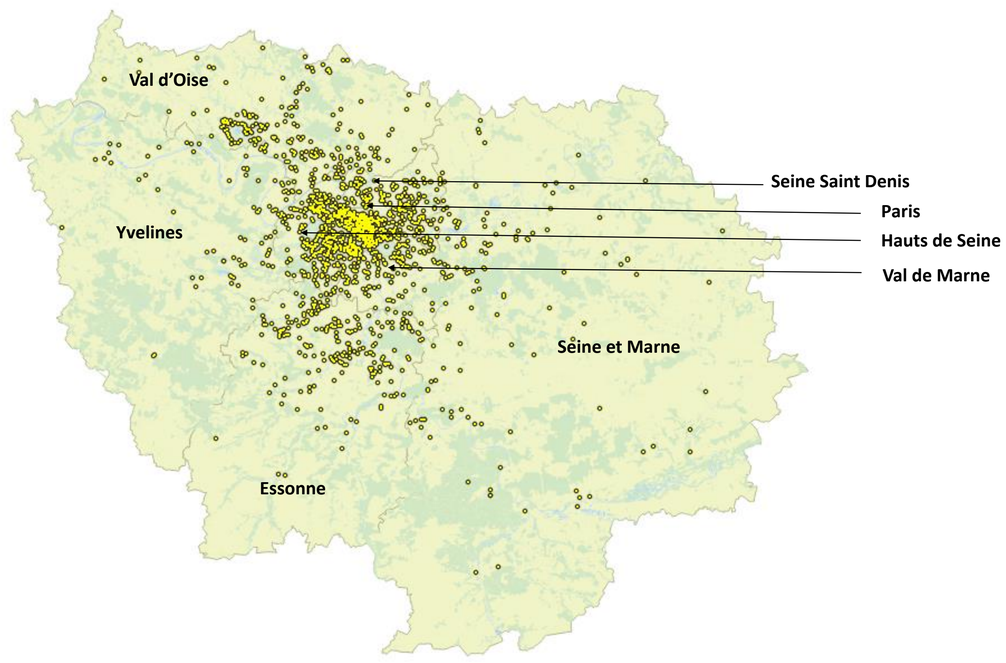

Figure 2: Impact of PM2.5 weekly exposure on multiple sclerosis relapse, multivariable analysis

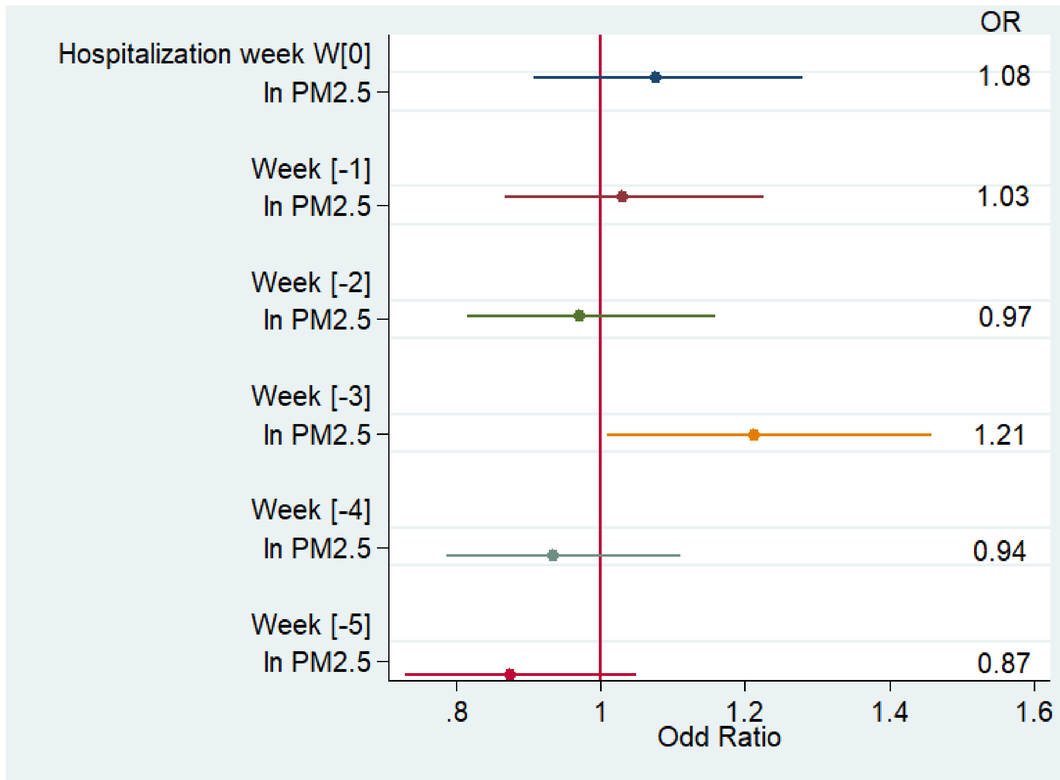

Figure 3: Impact of PM2.5 exposure during week[-3] on multiple sclerosis relapse, among different classes of age, multivariable analysis

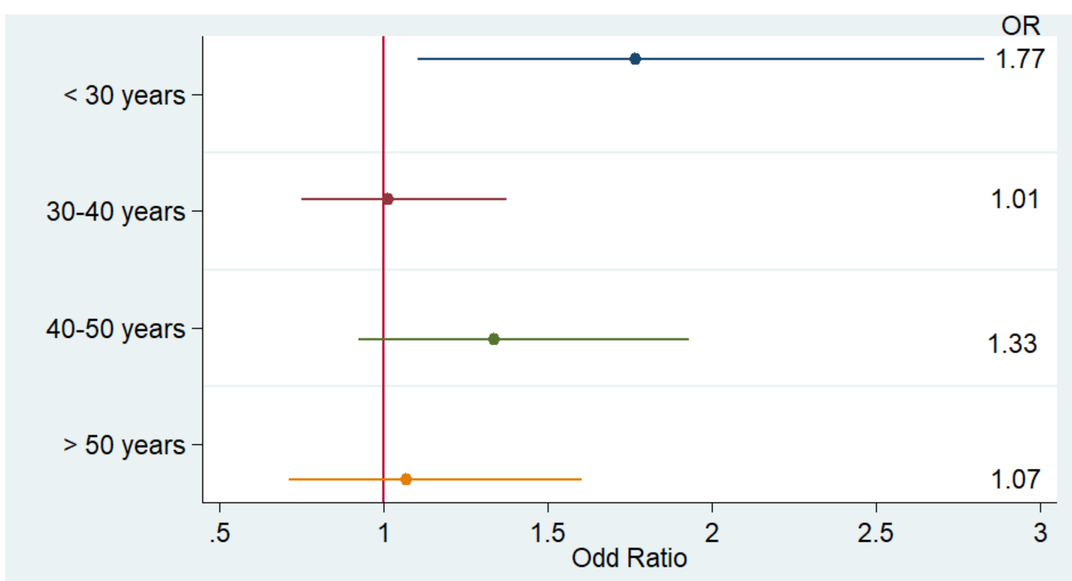

Table 2: Impact of PM2.5 weekly exposure during Week[-3] on multiple sclerosis relapse, multivariable analysis adjusted on average weekly temperature, flu like syndrome rate, pollen exposure, and holiday period.

Variable	Odd Ratio (CI 95%)	P value
Ln PM2.5	**1.21 (1.01;1.46)**	**0.039**
Weekly mean of dairy maximal temperature (1)	0.98 (0.86;1.13)	0.798
Weekly flu like syndrome rate (1)	1.05 (0.92;1.20)	0.457
Weekly pollen exposure (1)	0.94 (0.86;1.03)	0.189
Holliday period (2)	0.82 (0.60;1.13)	0.227

(1) By increase of one quartile (2) Holidays: Christmas and summer holidays

Discussion:

PM2,5 exposure during week[-3] before hospitalization was electively associated with multiple sclerosis relapse. In the verification subset made in Saint Antoine hospital (77 patients), week[-2] was the week when relapse symptoms appeared (median of delay between symptoms onset and hospitalization: 14 days [first quartile 7 days, third quartile 30 days]). PM2.5 could thus act as a trigger of multiple sclerosis relapse.

PM2.5 exposure effect was essentially observed among young people. Youth is associated with a more inflammatory disease(10), thus young people could be more sensitive to environmental toxicity. Moreover, young patients with multiple sclerosis may be more exposed than older, in particular in their journey from house to work, as self employment is extremely rapidly declining with aging in multiple sclerosis patients(11).

Conclusion:

PM2.5 exposure is associated with the risk of multiple sclerosis relapse.
The observed effect of PM2.5 is maximal among young people of less than 30 years.

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