Amyotrophic lateral sclerosis spatial epidemiology in the Mount Etna region, Italy

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Keywords: amyotrophic lateral sclerosis, motor neuron diseases, Mount Etna, spatial epidemiology, volcanogenic metals

doi:10.1111/ene.14011

Received: 24 April 2019
Accepted: 23 May 2019

Previously, we described a significantly higher risk of amyotrophic lateral sclerosis (ALS) among the population living on the eastern flank of Mount Etna with respect to the western flank [relative risk 2.75; 95% confidence interval (CI) 1.64–4.89] [1]. Since winds usually blow Etna ash from west to northwest [2], the eastern flank is the most exposed area and volcanogenic metals were proposed as a possible explanation.

Here, we further investigated the spatial distribution of ALS cases in the Mount Etna region during 2005–2015, performing a geostatistical cluster analysis. The study was conducted in the province of Catania. ALS patients were diagnosed according to the El Escorial revised criteria [3]. Standardized incidence ratios (SIRs) of each communality were calculated using the annual population of the entire province as a reference through an age- and sex-adjusted indirect standardization. Cluster analysis was performed using both a local Moran index (also termed Local Indicators of Spatial Association, LISA) [4] and Kulldorff's spatial scan statistics [5]. The Monte Carlo simulation was used to assess the statistical significance of the results (*P* value was set at 0.05%). The Kulldorff spatial scan statistic was implemented using SatScan software, version 9.4.4 [6].

A total of 202 residents were diagnosed with ALS during 2005–2015 giving a mean annual crude incidence rate of 1.70/100 000 person-years (95% CI 1.47–1.94) (Table S1). Two communalities, both located on the southeastern flank of the volcano, showed an SIR higher than 1 (SIR 1.80, 95% CI 1.07–2.84, and SIR 2.28, 95% CI 1.18–3.99) (Fig. 1a). LISA analysis showed the presence of an aggregative spatial structure on the southeastern flank of Mount Etna and Kulldorff's statistic confirmed the above indication by revealing a higher incidence spatio-temporal cluster that includes 13 communalities in the same area. During the 2006–2010 period, 13.24 cases were expected whereas 33 were observed, therefore resulting in an SIR of 2.49 (95% CI 1.72–3.50, *P* value 0.007) (Fig. 1b). Purely spatial analysis revealed a smaller cluster including four communalities, with an SIR of 2.2 (95% CI 1.39–3.3) (Fig. 1b).

Several genetic and environmental factors have been proposed to play a role in the ALS pathogenesis. Among environmental factors, metals seem to play a relevant role [7]. Volcanoes are a major source of metals [8] and Mount Etna is the largest active volcano in Europe. We found a higher incidence spatio-temporal cluster (2006–2010) on the southeastern flank of the volcano, the area most exposed to volcanic ash. In fact, during 2001–2003 an intense and long-lasting explosive activity of Mount Etna was recorded from eruptive fissures located on the southern and the eastern flanks of the volcano and during this period about 2.1 kg/m^2 of ash was deposited in 3 days [9].

This finding could further suggest the possible role of volcanogenic metals in ALS pathogenesis. Nonetheless, we cannot exclude that other factors, both genetic and environmental, may have contributed to the higher incidence of ALS on the southeastern flank of Mount Etna. Further studies are needed in order to explore possible alternative hypotheses.

Acknowledgements

This research was funded by the Department of Medical and Surgical Sciences and Advanced Technologies 'GF Ingrassia', University of Catania, Italy (Piano Triennale di Sviluppo delle Attivita' di Ricerca Scientifica del Dipartimento 2016–18).

Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Table S1. Age- and sex-specific incidence rate (IR) in the province of Catania.

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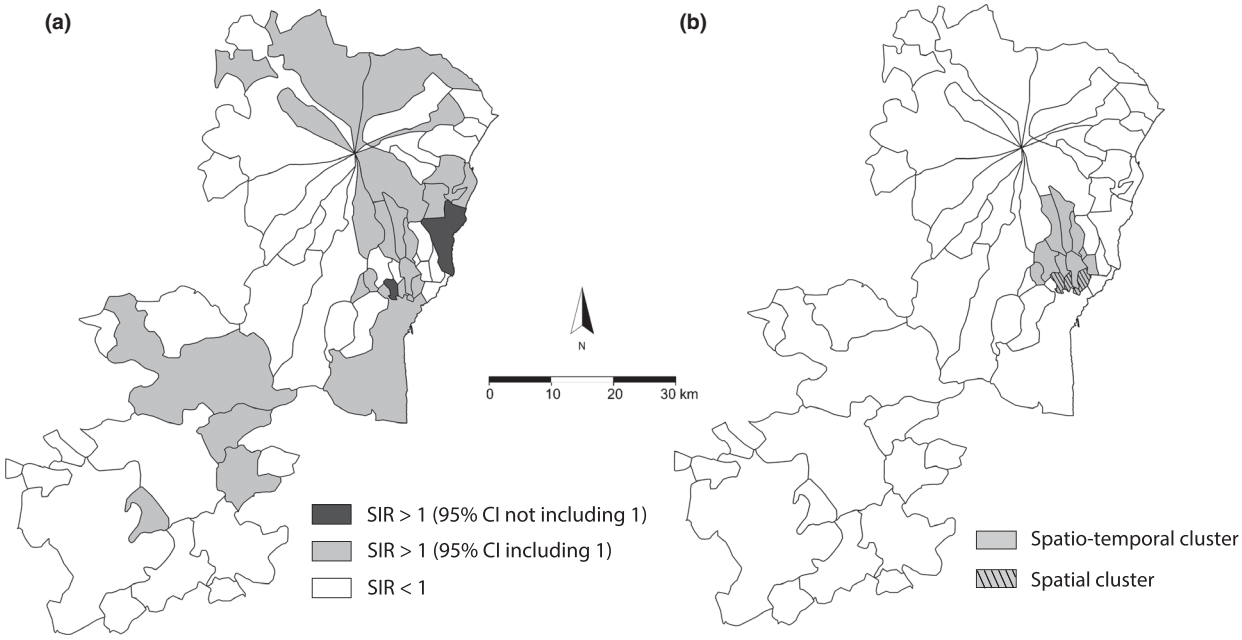

Figure 1 (a) Communalities' SIRs in the province of Catania. (b) The spatio-temporal and purely spatial high-incidence clusters revealed by the Kulldorff's statistic.

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