Hyperosmia in Lyme disease
Hyperosmia na doença de Lyme
Basant K. Puri1, Jean A. Monro2, Peter O. O. Julu1,2,3,4,5,6, Michele C. Kingston2, Mussadiq Shah2,3,4,5

ABSTRACT
Neurological involvement in Lyme disease has been reported to include meningitis, cranial neuropathy and radiculoneuritis. While it is known that in some cases of aseptic meningitis patients may develop hyperosmia, the association between hyperosmia and Lyme disease has not previously been studied. **Objective:** To carry out the first systematic study to ascertain whether hyperosmia is also a feature of Lyme disease. **Method:** A questionnaire regarding abnormal sensory sensitivity in respect of the sense of smell was administered to 16 serologically positive Lyme disease patients and to 18 control subjects. **Results:** The two groups were matched in respect of age, sex and body mass. None of the 34 subjects was suffering from migraine. Eight (50%) of the Lyme patients and none (0%) of the controls suffered from hyperosmia (p=0.0007). **Conclusion:** This first systematic controlled study showed that Lyme disease is associated with hyperosmia.

Keywords: olfaction, hyperosmia, Lyme disease.

RESUMO
Tem sido descrito acometimento neurológico na doença de Lyme: meningite, neuropatia de nervos cranianos, e radiculoneurite. É bem conhecida a ocorrência de hiperosmia em alguns casos de meningites assépticas, mas a associação de hiperosmia com doença de Lyme ainda não foi relatada. **Objetivo:** Conduzir um estudo sistemático para investigar se a hiperossmia é característica também da doença de Lyme. **Método:** Foi aplicado um questionário pesquisando a ocorrência de sensibilidade anormal em relação ao sentido da olfação a 16 pacientes com sorologia positiva para doença de Lyme e a 18 controles normais. Os dois grupos foram pareados em relação a idade, sexo e massa corporal. Nenhum dos 34 sujeitos sofria de enxaqueca. **Resultados:** Foi detectada hiperossmia em 8 sujeitos com doença de Lyme (50%) enquanto que a hiperosmia não apareceu em nenhum sujeito do grupo controle (p=0,0007). **Conclusão:** Doença de Lyme está associada à hiperossmia.

Palavras-chave: olfação, hiperossmia, doença de Lyme.

The study was carried out at: Breakspear Medical Group, Hemel Hempstead, UK. B. K. Puri, MA, PhD, MB, BChir, BSc (Hons) MathSci, DipStat, PG Dip Maths, MMath, FRCPsych, FSB; Consultant Psychiatrist (Hammersmith Hospital), Adjunct Professor in Neuroimaging and Spectroscopy (UL); J. A. Monro, MB, BS, MRCS, LRCP, FAAEM, DIBEM, MACOEM; Medical Director of Breakspear Medical Group; P. O. O. Julu, MB, ChB, MSc, PhD; Senior Clinical Research Fellow (Imperial College London), Consultant Physician and Specialist Autonomic Neurophysiologist (Breakspear Medical Group), Consultant Autonomic Neurophysiologist (Queen Mary University of London), Consultant Neurophysiologist in Charge (National Rett Center, Frösön); M. C. Kingston, BA (Hons), BSc Nutri Med, mBANT; Clinical Nutritionist (Breakspear Medical Group); M. Shah, BSc, MSc, PhD; Clinical and Autonomic Neurophysiologist (Breakspear Medical Group), Senior Lecturer in Sensory System (Queen Mary University of London).

Olfaction is still poorly understood in humans; the main disorder of olfaction is anosmia or loss of the sense of smell1. Patients with hyperosmia complain of having an increased sensitivity of the sense of smell.

Lyme disease (also known as Lyme borreliosis) is a systemic arthropod-borne zoonosis caused by Borrelia spirochaetes, the incidence of which has recently been increasing with the geographical spread of infected ticks. It is well established that the bacteria can invade the skin (causing erythema migrans), musculoskeletal system (giving rise to Lyme arthritis), cardiovascular system (causing Lyme carditis) and the nervous system (Lyme neuroborreliosis).
which may be associated with neuropsychiatric symptomatology\textsuperscript{2}. In particular, neurological involvement in Lyme disease has been reported to include meningitis, cranial neuropathy and radiculoneuritis. It is known that in some cases of aseptic meningitis patients may develop hyperosmia\textsuperscript{3}. However, to date, there have been no published studies regarding the relationship between Lyme disease and hyperosmia.

Therefore, the objective was to carry out the first systematic study to ascertain whether hyperosmia is a feature of Lyme disease.

**METHOD**

**Subjects**

This study was cross-sectional. Serologically positive Lyme disease patients attending the neuroscience department were included in the study if they were aged 18 years or over, but excluded from the study if they were suffering from migraine or if they had suffered olfactory lesions.

Written informed consent was obtained and the AONM research ethics committee approved the study under protocol number 003-2012. All participants signed an informed consent form before taking part in this study. The study was carried out in accordance with the Declaration of Helsinki.

**Procedures**

The date of birth, sex, body mass and past medical history of each subject were recorded. Each subject was asked whether or not he or she was unduly sensitive to odours.

**Statistical analysis**

Continuous variables for which data which did not differ significantly from normality and for which the two groups did not have significantly different variances were compared between the Lyme disease and control groups using independent samples \( t \)-tests (equal variances), while discrete nominal variables were compared between groups using Fisher’s exact probability test. All tests were two-tailed.

The software package used for the statistical analyses was IBM SPSS Statistics for Windows, Version 21.0.0.0 (64-bit edition) (IBM Corp, Armonk, NY, USA).

**RESULTS**

Sixteen serologically positive Lyme disease patients and 18 control subjects were studied. The two groups were matched in respect of mean age, sex ratio and mean body mass, as shown in Table.

Eight (50\%) of the Lyme disease patients and none (0\%) of the controls suffered from hyperosmia (Fisher’s exact probability test, \( p = 0.0007 \)).

**DISCUSSION**

This first systematic controlled study showed that Lyme disease is associated with hyperosmia. In the sample studied, there was a highly significant prevalence of hyperosmia in Lyme disease of 50\%.

Known migraineurs were excluded from this study and so it is unlikely that migraine could account for our finding. Again, as none of the subjects included in the study had clinical signs of meningitis, it is unlikely that meningitis could account for the high prevalence of hyperosmia in the Lyme disease group, although a subclinical form of meningitis associated with Lyme borreliosis cannot be ruled out as of importance. Finally, it should be noted that none of the medication taken by any of the patients is known to be associated with hyperosmia.

This is the first study of hyperosmia in Lyme disease. The high prevalence of this olfactory disorder found in our study suggests the need for further studies of olfactory function in this disease. It would also be of interest to carry out longitudinal studies to evaluate the response of hyperosmia to antibiotic pharmacotherapy.

**Table.** Mean age, sex and mean body mass of Lyme disease patients and controls; standard errors are given in parentheses.

<table>
<thead>
<tr>
<th></th>
<th>Lyme disease n=16</th>
<th>Controls n=18</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y)</td>
<td>36.8 (4.1)</td>
<td>45.2 (3.9)</td>
<td>0.144*</td>
</tr>
<tr>
<td>Sex</td>
<td>6 males,</td>
<td>7 males,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 females</td>
<td>11 females</td>
<td></td>
</tr>
<tr>
<td>Mean body mass (kg)</td>
<td>25.2 (1.2)</td>
<td>24.6 (0.8)</td>
<td>0.666*</td>
</tr>
</tbody>
</table>

\*Independent samples \( t \)-test; \textsuperscript{1}Fisher exact probability test.

**References**