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# Obstructive sleep apnea syndrome and olfactory perception: An OERP study

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ABSTRACT

Obstructive Sleep Apnea Syndrome (OSA) is characterized by snoring associated with repeated apnea and/or obstructive hypopnea. The nasal airways of OSA patients, measured via acoustic rhinometry, could be significantly narrower than healthy subjects and this reduced nasal structure can impair olfactory function. The relationship between nasal structure and olfactory function, assessed via behavioral test results, indicates that there is a high prevalence of nasal airflow problems. Based on these assumptions, the purpose of this study was to carry out an assessment of olfactory perception in OSA patients through the Chemosensory Event-Related Potentials (CSERP), investigating the N1 component and the Late Positive Component (LPC). Twelve OSA patients, non-smokers, were recruited in the Pulmonary Rehabilitation Unit, scored with the Epworth Sleepiness Scales, after Polygraphic Recording, Apnea Hypopnea Index and Body Mass Index evaluation. The control group consisted of twelve healthy controls, non-smokers, recruited as volunteers. Subjects, during an EEG recording, performed an oddball olfactory recognition task based on two scents: rose and eucalyptus. Main results highlighted differences in N1 and LPC between OSA and controls. OSA patients presented faster N1 latencies and greater amplitude. The same trend was found in LPC, where OSA showed decreased latency and increased amplitude during rose stimulation, in the right inferior frontal cortex. and faster latencies in left centroparietal cortex OERP results can suggest an impairment in endogenous components. This result could be the consequence of the exogenous perceptual difficulty highlighted in N1 component. The increased arousal could also be related to the respiratory activity involved during the olfactory task.

## 1. Introduction

Obstructive Sleep Apnea (OSA) is a respiratory disorder characterized by frequent snoring associated with repeated apnea and/or obstructive hypopnea, e.g., respiratory breaks lasting more than 10 s, caused by a partial or complete blockage of the high airways (Gutierrez et al., 2013; Punjabi, 2008). Obstructive Sleep Apnea syndrome is diagnosed according to the criteria of American Academy of Sleep Medicine (AASM) classification (Kapur et al., 2017). OSA causes daytime sleepiness, mood problems, poor neurocognitive performance, limited quality of life, and cardiometabolic disorders (Beebe, 2006). The neurocognitive dysfunctions due to OSA affect long-term memory and learning (Gagnon et al., 2014), attention and executive functions (Jackson et al., 2011). Olfactory function is influenced by cognitive dysfunctions as well as by other major factors such as head trauma, respiratory infections and sinonasal disorders (Hedner et al., 2010). Several studies have also shown that the decrease in olfactory responses could be a cue in some cognitive impairment diseases, such as Mild Cognitive Impairment and Alzheimer's (Masurkar and Devanand, 2014; Roberts et al., 2016).

However, there are few studies on the relationship between the effect of olfactory function and severity of OSA, although it is evident that in this disorder there is an involvement of peripheral respiratory functions as well as upper airway muscles (Gutierrez et al., 2013;

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Shigeta et al., 2010). The nasal airways of OSA patients, measured via acoustic rhinometry, could be significantly narrower than healthy subjects', and this relatively narrow nasal structure can reduce olfactory function. Boerner et al. (2017) and Salihoğlu et al. (2014) examined the relationship between nasal structure and olfactory function via acoustic rhinometry and the Sniffin' Sticks test (Kobal et al., 1996), and found that there is a high prevalence of nasal airflow problems in OSA patients.

Sniffin' Sticks test is a behavioural test on olfactory perception, based on the assessment of olfactory threshold, and of smell discrimination and identification. It is based on pen like odor dispensing device (Hummel et al., 1997).

Following up on these results, the purpose of this study was to investigate olfactory perception in OSA patients, and to carry out an objectively quantifiable olfactory assessment in OSA through the registration of chemosensory (i.e., olfactory) event-related potentials (CSERP) (Pause and Krauel, 2000). To assess CSERP, we administrated two different odorants (i.e, rose and eucalyptus) (Hummel et al., 2009), during an Oddball paradigm (Pause et al., 1996b). Oddball paradigm is a classical paradigm used in psychology and in electrophysiology, able to elicit ERP components. During the oddball task, sensorial frequent stimuli (Non-Target) are interrupted by infrequent stimuli (Target). The stimulation can be administrated via different sensorial modalities (e.g., acoustic, visual, olfactory, nociceptive and so on). This paradigm is often used in the clinic to investigate dysfunctions in perceptive or cognitive processing (Polich and Margala, 1997). The study of olfactory assessment through CERPs is extremely important because, in this case, it is possible to evaluate the functional aspects, the timing, and the intensity of processing related to the stimuli administered. Furthermore, in this research, the presentation of olfactory stimuli was quantitatively controlled both in time and in intensity, and exactly triggered and time locked on the EEG track (Invitto et al., 2017a,b).

## 2. Methods

### 2.1. Subjects

We conducted the experimental research in the DREAM Neuroscience Laboratory in Vito Fazzi Hospital in Lecce, Italy. Data collection was performed in accordance with the Helsinki Declaration, and written informed consent was obtained from all participants. This study was carried out in accordance with the recommendations of Ethical Committee of Vito Fazzi Hospital, Lecce (Italy). All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Ethical Committee of Vito Fazzi Hospital, Lecce (Verbal N.36 – 13-05-16). OSA and Control groups were recruited in a temporal range between October 2016 and July 2017.

Twelve OSA patients (4 women and 8 men; mean age 53 years; SD ± 12.46), non-smokers, were enrolled with a clinical suspicion of OSA and were admitted to the Department of Rehabilitation, Cardiorespiratory Rehabilitation Unit, ASL Lecce, Italy, to perform the sleep study. The patients recruited in the study were chosen to have a sample that could reflect the disorder without severe comorbidities (e.g., diabetes mellitus). OSA was confirmed by polygraphic recording evaluation with an apnea index (AHI) of > 5 apneas/hour of sleep according to the diagnostic criteria of the AASM (Kapur et al., 2017). The definition of apnea and hypopnea was based on standard criteria (Berry et al., 2012). Portable Monitoring (PM) is used as an alternative to polysomnography (PSG) for OSA diagnosis (Cooksey and Balachandran, 2016; Corral et al., 2017). For appropriately selected outpatients, evidence is accumulating that PM are a reasonable substitute for in-laboratory polysomnography. Indices of oxygen saturation, snoring, air flow, thoracic and abdominal respiratory movements, heart rate, including ECG in real-time mode, and body position were assessed polygraphically (i.e., Embletta pds, Recording System, Broomfield, CO, USA). Each recording was performed between 11:00 pm and 6:00 am. The signals, which were saved in a digital recorder, were computer-analysed, and validated by the physician, the morning after the recording. In addition, the following parameters were investigated: Mean nocturnal $SaO_2$%, nocturnal Nadir $SaO_2$%. Mean nocturnal $SaO_2$% was defined as a $SaO_2$ of < 90% for at least 5 min with a $NSaO_2$ of ≤ 85%. Time in bed was defined as the time interval from the start to the end of the recording.

Obesity was diagnosed when Body Mass Index (BMI) > 29.9 $kg/m^2$. Subjective assessment of daytime sleepiness was carried out using the Epworth Sleepiness Scale (ESS) (Johns, 1991).

The OSA patients were visited by an ENT doctor. The fiberoptic endoscopy highlighted: nasal obstruction due to deformity of the septum; reductions in pharyngeal lumen size that increase collapsibility; a history of snoring for at least two years and chronic rhinosinusitis (CRS). Seven OSA patients took antihypertensive drug therapy.

Twelve healthy participants, matched by age (5 women and 7 men; mean age 51 years; SD ± 1.73), non-smokers, with spontaneous participation were recruited from volunteer adult subjects.

ENT investigation in Control group didn't highlight otorhinolaryngological diseases. Furthermore, they didn't report any chronic diseases and they did not take drugs.

The Parameters of OSA and Control Group are indicated in Table 1.

### 2.2. Chemosensory event related potentials task

Subjects performed an olfactory recognition task involving two odors: Rose and Eucalyptus. The vials were administered via an olfactometer interfaced within EEG (Invitto et al., 2014). Each CSERP task was performed within one month from the subject's polygraphic recording.

Odorant stimuli were chosen according to the literature (Hummel et al., 2009): phenylethyl alcohol (rose odor perception, β-PEA, 2-Phenylethanol, CAS Number: 60-12-8, Number W285803 Sigma - Aldrich) and Eucalyptol (eucalyptus odor perception, 1,3,3-Trimethyl-2-oxabicyclo[2.2.2]octane, CAS Number: 470-82-6, Number C80601 Sigma-Aldrich). The experimental concentration of PEA is 20 µL in 10 mL of Vaseline Oil [CnH(2n + 2)]. The odorous solutions were put into 20 mL transparent glass vials. The laboratory's internal temperature was kept constant at 25 C°. The smells were kept in a darkened cabinet and were kept sealed with plastic film.

The presentation paradigm was an oddball task (Polich and Margala, 1997) adapted to olfactory task (see Fig. 1). Each stimulation lasted 450 ms, the duration of the Interstimulus Interval (ISI) was 60 s, and the total duration of the task was about 40 min. In accordance with recommendations based on prior research, the ISI was longer than 10 s to avoid olfactory habituation (Pause et al., 1997). This allows a non-accustomed response even for cognitive elaboration, where the cognitive processing time of the olfactory stimulus occurs, in OERPs, with slow potentials, within the range of 600 ms (Invitto et al., 2017b).

The device that allows recording of odorous stimuli presentation allows measuring the CSERPs evoked by olfactory stimuli in a controlled, automated mode synchronized to the acquisition of the EEG signal. The presentation is conveyed through a plexiglas tube in a black

**Table 1**
Descriptive Values of OSA and Controls.

| Variables | OSAS patients | Control subjects |
|---|---|---|
| Number of subjects | 12 (9 m; 3 w) | 12 (7 m; 5 w) |
| Age (years) | 53. ± 12.46 | 51 ± 1.73 |
| BMI ($kg/m^2$) | 33.3 ± 6.43 | 23.17 ± 2.28 |
| Epworth Sleepiness Scale score | 12.58 ± 1.78 | 7.08 ± 0.90 |
| Mean Nocturnal $SaO_2$% | 91.43 ± 3.43 | 97.64 ± 0.67 |
| Nocturnal Nadir $SaO_2$% | 81.45 ± 2.24 | 90.45 ± 1.09 |
| Apnea/hypopnea index | 38.54 ± 16.35 | 1.26 ± 0.96 |

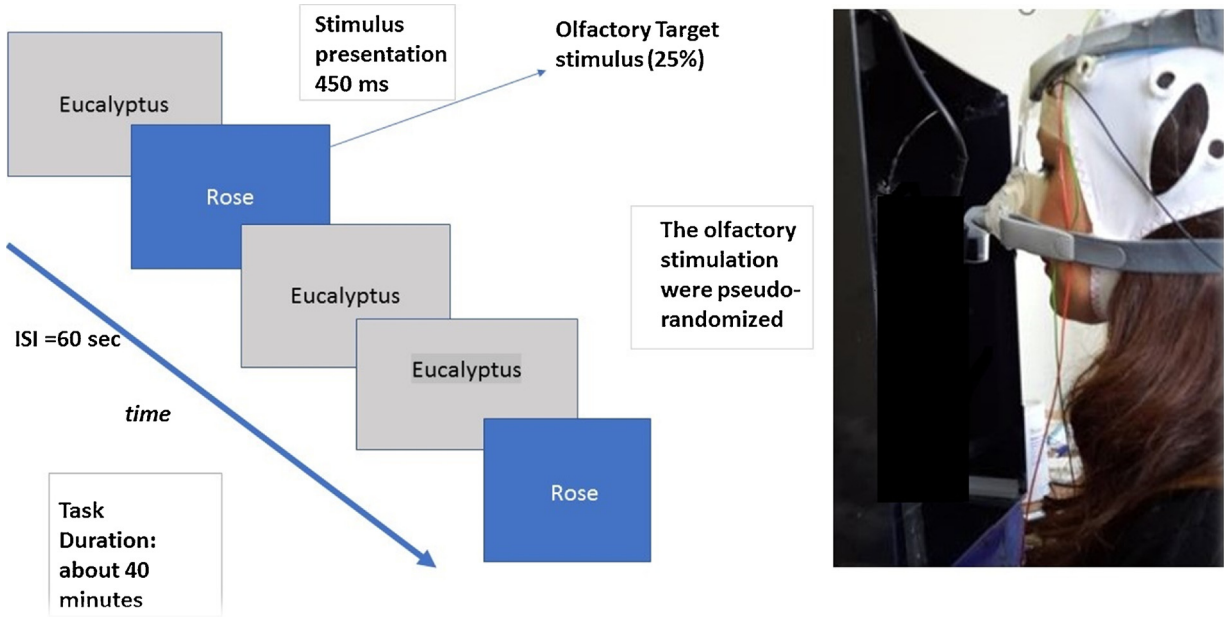


**Fig. 1.** Example of an Olfactory oddball task (i.e, Rose and Eucalyptus stimuli) during an EEG recording.

**Table 2**
Results of linear mixed-effects model: Fixed effects for group and odor on Amplitude (N1).

| Electrode | | $\chi^2$(df) | B(SE) | t |
|---|---|---|---|---|
| F8 | Baseline | | −3.677(1.05) | −3.47 |
| | **Group** | 4.942(1)* | | |
| | Controls vs. OSA | | −3.80(1.39) | −2.17* |
| | **Odor** | 366.526(1)*** | | |
| | Eucalyptus vs. Rose | | 1.629(0.19) | 8.38*** |
| | **Group x Odor** | 30.171(1)*** | | |
| | Controls x Eucalyptus vs. OSA x Rose | | 1.412(0.25) | 5.49*** |

Notes: Subjects were treated as random effects, degrees of freedom of the model were calculated with the Satterthwaite approximation. Values of $\chi^2$ are computed with the type-II Wald test. $N_{obs}$ = 588, $N_{groups}$ = 21.
*p < .05, ***p < .001.

**Table 3**
Results of linear mixed-effects model: Fixed effects for group and odor on Latency (N1).

| Electrode | | $\chi^2$(df) | B(SE) | t |
|---|---|---|---|---|
| F8 | Baseline | | 546.278(53.46) | 10.21 |
| | **Group** | 5.759(1)* | | |
| | Controls vs. OSA | | −92.722(32.45) | −2.85** |
| | **Odor** | 87.47*** | | |
| | Eucalyptus vs. Rose | | −58.444(6.64) | −8.79*** |
| | **Group x Odor** | 12.537*** | | |
| | Controls x Eucalyptus vs. OSA x Rose | | 31.111(8.78) | 3.54*** |

Notes:Subjects were treated as random effects, degrees of freedom of the model were calculated with the Satterthwaite approximation. Values of $\chi^2$ are computed with the type-II Wald test. $N_{obs}$ = 588, $N_{groups}$ = 21.
* p < .05.
** p < .01.
*** p < .001.

cave that avoids the presentation of visual stimuli. The air flow, after collecting the volatile components of the substances S1 and S2, transfers them to an exposure open box (a black cave), where the subject enters his head. To avoid visual constraints, the cave has been appropriately obscured. Furthermore, this method allows a blind presentation of smells (Invitto et al., 2015, 2017a,b).

**Table 4**
Results of linear mixed-effects model: Fixed effects for group and odor on Amplitude (LPC).

| Electrode | | $\chi^2$(df) | B(SE) | t |
|---|---|---|---|---|
| F8 | Baseline | | 1.419(0.65) | 2.17 |
| | **Group** | 10.649(1)** | | |
| | Controls vs. OSA | | −3.181(0.86) | −3.68** |
| | **Odor** | 634.55(1)*** | | |
| | Eucalipto vs. Rose | | −3.466(0.18) | −18.95*** |
| | **Group x Odor** | 10.655(1)** | | |
| | Controls x Eucalipto vs. OSA x Rose | | 0.789(0.24) | 3.26** |

Notes: Subjects were treated as random effects, degrees of freedom of the model were calculated with the Satterthwaite approximation. Values of $\chi^2$ are computed with the type-II Wald test. $N_{obs}$ = 588, $N_{groups}$ = 21.
**p < .01, ***p < .001.

### 2.3. CSERP recording

EEG signals were recorded from a 16 channels amplifier (Brain Products V-Amp) mounted in an electrode cap according to the International 10–20-system. We used the Brain Vision Recorder recording software and the Brain Vision Analyzer (Brain Products GmbH) analysis software. Electrode impedance was kept below 15 kΩ. The EEG recording sampling rate was 500 Hz. Electrodes were referenced online to the FcZ (Nuwer et al., 1994). One electrode was placed at the outer canthus of the right eye and used to monitor eye movements. Trials contaminated by eye movements, amplifier conditioning, or other artifacts were rejected. The signal was filtered offline (0.01–50 Hz, 24 dB), and the threshold for artifact rejection was set at > |125|μV (Pause et al., 1997) (Pause et al., 1996). Ocular rejection was performed through independent component analysis (ICA). ERP epochs included a 100-ms pre-stimulus baseline period and a 500-ms post-stimulus segment. Separate averages were calculated for each odorant segmentation (rose and eucalyptus). Peaks detection were applied according to previous studies (Invitto et al., 2017a,b).

**Table 5**
Results of linear mixed-effects model: Fixed effects for group and odor on Latency (LPC).

| Electrode | | $\chi^2$(df) | B(SE) | t |
|---|---|---|---|---|
| F8 | Baseline | | 253.11(20.28) | 12.47 |
| | **Group** | 6.524(1)* | | |
| | Controls vs. OSA | | −73.61(26.83) | −2.74* |
| | **Odor** | 1169.65(1)*** | | |
| | Eucalyptus vs. Rose | | 142.00(6.64) | 21.35*** |
| | **Group x Odor** | 1.861(1) | | |
| | Controls x Eucalyptus vs. OSA x Rose | | 12.00(8.79) | 1.36 |
| C3 | Baseline | | 263.77(24.18) | 11.07 |
| | **Group** | 5.418(1)* | | |
| | Controls vs. OSA | | −95.78(32.00) | −2.99** |
| | **Odor** | 1206.6(1)*** | | |
| | Eucalyptus vs. Rose | | 154.88(7.93) | 19.52*** |
| | **Group x Odor** | 18.07(1)*** | | |
| | Controls x Eucalyptus vs. OSA x Rose | | 44.61(10.49) | 4.25*** |

Notes: Subjects were treated as random effects, degrees of freedom of the model were calculated with the Satterthwaite approximation. Values of $\chi^2$ are computed with the type-II Wald test. $N_{obs}$ = 588, $N_{groups}$ = 21.
* p < .05.
** p < .01.
*** p < .001.

## 3. Analysis and results

Statistical analyses were performed using linear mixed-effects models (LMMs) of the lme4 package (Bates et al., 2015) supplied in the R environment for statistical computing (version 3.1.1). In the current study, we first analyzed all the electrodes in a unique linear model by defining a ROIs categorical variable. The results did not show any significance for ROIs. Next, we analyzed each electrode, analyzing amplitude and latency for each significant electrode (Luck and Gaspelin, 2016) as reported in Tables 2–5.

### 3.1. Amplitude and latency of N1 component

The analyses of effects revealed significant effects, in the F8 electrode, for Group ($\chi^2_1$ = 4.94, p = .02), Odor ($\chi^2_1$ = 366.52, p < .001), and the interaction Group x Odor ($\chi^2$(1 = 30.17, p < .001) (Table 2). The Group effect showed a greater N1 amplitude in OSA group (B = -3.80, $t_{19}$ = -2.17, p = .01); smell condition showed a significant effect in the direction of a decreased amplitude during Rose condition (B = 1.62, $t_{565}$ = 8.38, p < .001); the interaction highlighted in the OSA group an increased N1 in the Rose condition (B = 1.41, $t_{565}$ = 5.49, p < .001) (Table 2; Fig. 2).

The analyses of effects in N1 Latency revealed significant effects of Group ($\chi^2_1$ = 5.75, p = .002), Odor ($\chi^2_1$ = 87.47, p < .001), and the interaction Group x Odor ($\chi^2_1$ = 12.53, p < .001) (Table 3; Fig. 3).

Latency decreased in the OSA group (B = -92.72, $t_{19}$ = -2.85, p = .009) and in the Rose condition (B = -58.44, $t_{565}$ = -8.79, p < .001). Interaction showed a delayed latency in the OSA group in Rose Condition (B = 31.11, $t_{565}$ = 3.54, p < .001) (Figs. 4 and 5).

### 3.2. Amplitude and latency of LPC component

Amplitude analysis revealed significant effects in F8 for Group ($\chi^2_1$ = 10.64, p = .002), Odor ($\chi^2_1$ = 634.55, p < .001), and the interaction Group x Odor ($\chi^2_1$ = 10.65, p = .002) (Table 4). Group results highlighted a lower LPC in the OSA group (B = -3.18, $t_{19}$ = -3.68, p = .001); the odor condition highlighted a higher amplitude for the Rose Odorant (B = -3.46, $t_{565}$ = -18.95, p < .001). The significant interaction demonstrated a greater late Component in the OSA group (B = 0.78, $t_{565}$ = 3.26, p = .001) (Fig. 6).

With regards to F8 latency, the analysis revealed significant effects for Group ($\chi^2_1$ = 6.52, p = .01) and Odor ($\chi^2_1$ = 1169.65, p < .001), but there was not a significant interaction (Table 5). The Group effect was in the direction of higher Latency in the OSA group (B = -73.61, $t_{20}$ = -2.74, p = .01) and the effect for the Odor Condition involved a higher level for the Rose Odorant (B = 142, $t_{565}$ = 21.35, p < .001) (Fig. 7).

Considering the C3 electrode, we observed significant effects for

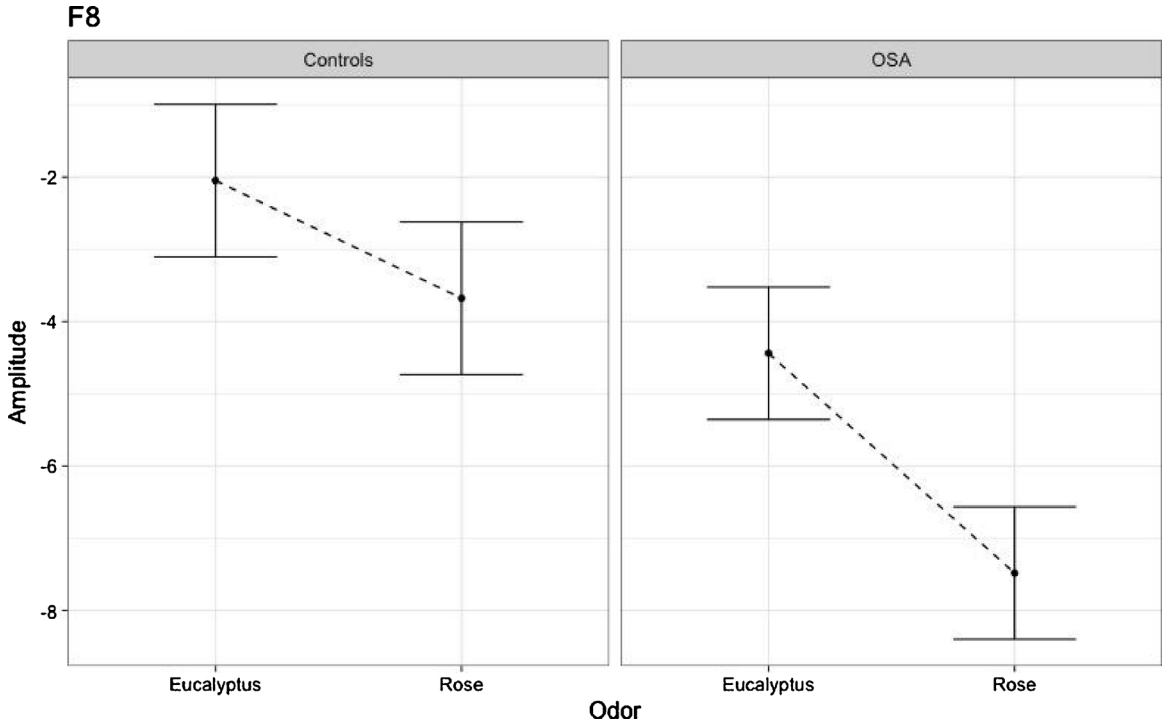


**Fig. 2.** N1 Averaged Amplitude in F8 Electrode in OSA and in Healthy Subjects for Rose and Eucalyptus Smell.

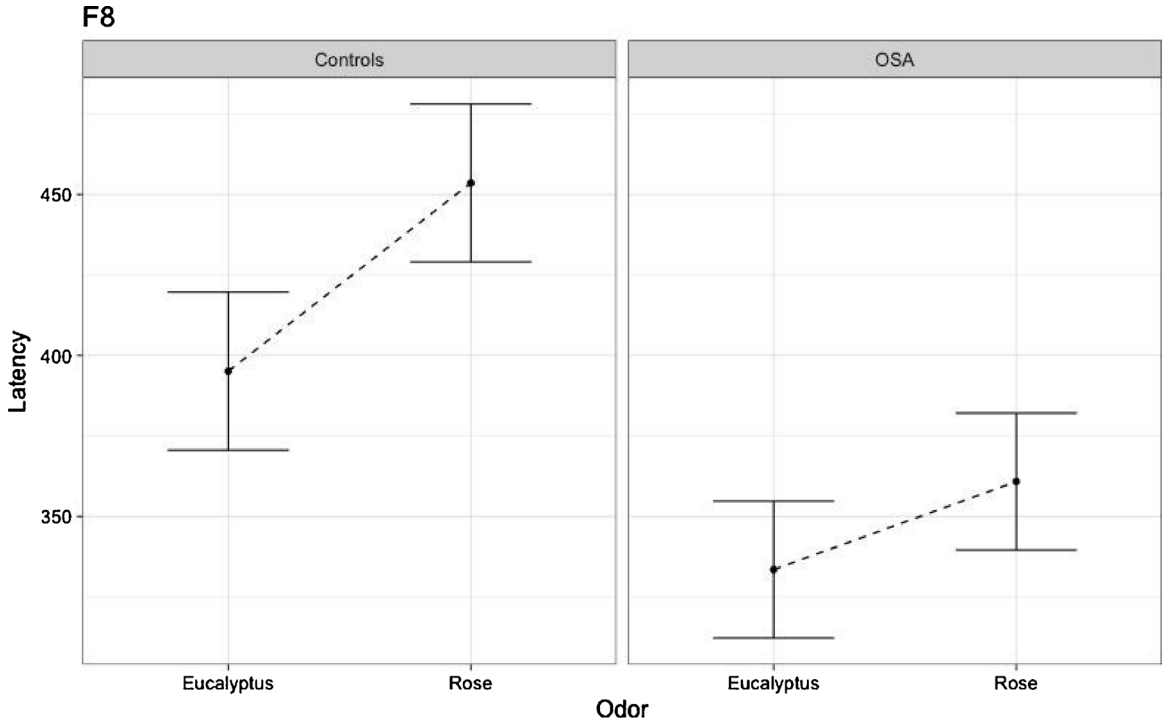


**Fig. 3.** N1 Averaged Latency in F8 Electrode in OSA and in Healthy Subjects for Rose and Eucalyptus Smell.

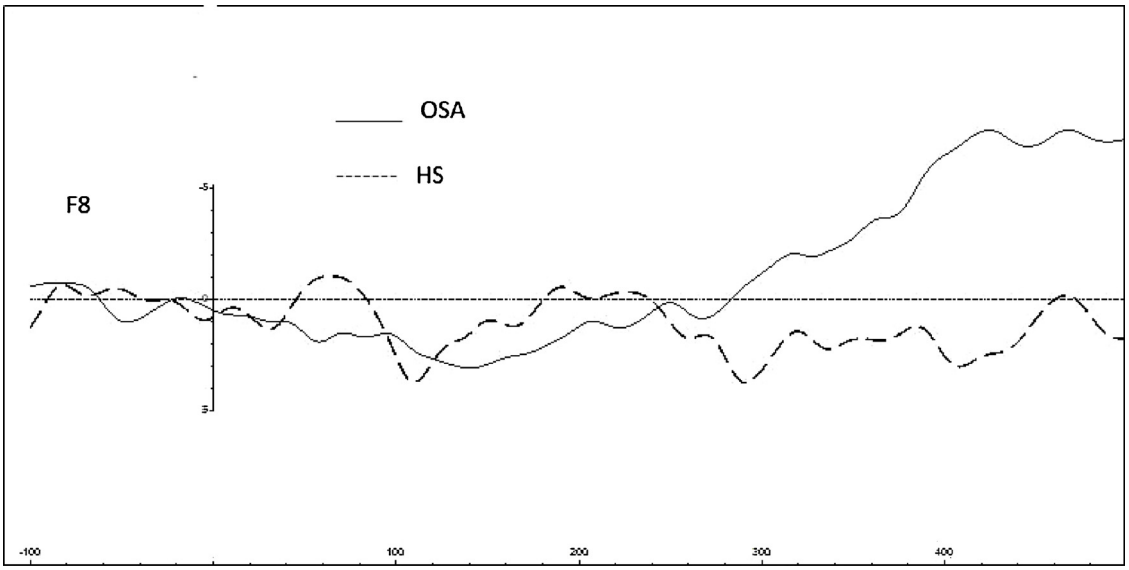


**Fig. 4.** Grand Average (F8 electrode): Matching CSERP response to Rose odorant in OSA patients (continuous Line) vs Healthy Subjects (dashed Line).

Group ($\chi^2_1 = 5.41$, $p = .001$), Odor ($\chi^2_1 = 1206.62$, $p < .001$), and Group x Odor ($\chi^2_1 = 18.07$, $p < .001$) (Fig. 8). Latency was delayed in the OSA group ($B = -95.78$, $t_{20} = -2.99$, $p = .007$); same trend was found in Rose Odorant condition ($B = 154.88$, $t_{565} = 19.52$, $p < .001$). The interaction resulted from decreased Latency in the OSA group during Rose stimulation ($B = 44.61$, $t_{565} = 4.25$, $p < .001$).

## 4. Discussion

Recent research investigated olfactory impairment in OSA disease, but this evidence was analyzed through behavioral tests (i.e., Sniffin Stick Test) or analyzed by non-functional neuroimaging technique (i.e., MRI), that in these studies are exclusively related to the peripheral examination of the olfactory bulb. The innovative aspect of this research is to use a method that allows a quantitative assessment of the sensorial and perceptive olfactory response.

Our result highlights significant differences in two CSERP components: a negative component (N1)(Rombaux et al., 2009), and a late positive component (LPC) (Pause et al., 1996). LPC usually is observed about 400–500 ms. post stimulus presentation. LPC, in OERP, has not been interpreted as a cognitive slow potential (Birbaumer, 1999; Donald, 2007), but the slow latency is interpreted as the physiological time due to sensorial and perceptive responses after an olfactory stimulation (Iannilli et al., 2017; Pause et al., 1996). In olfactory tasks, it has been demonstrated that it depends on subjective stimulus significance and it has been referred to as an endogenous component.

In the OSA and Control groups, we investigated N1 and LPC for both odorant conditions (rose and Eucalyptus). According to the oddball

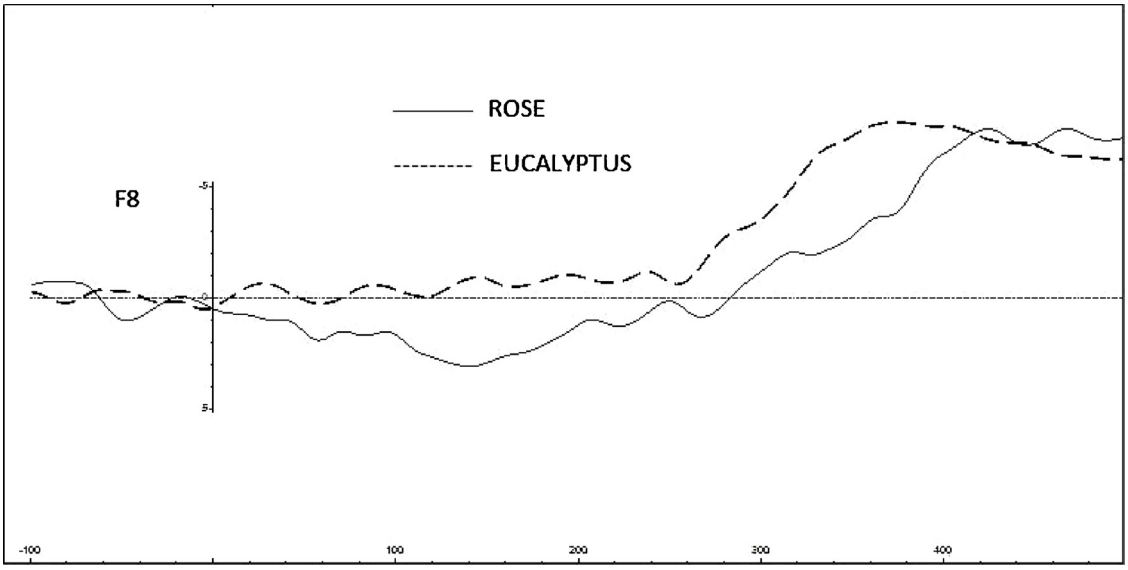


**Fig. 5.** Grand Average (F8 electrode): Matching CSERP response to Rose (Black Line) Vs Eucalyptus (Red Line) in OSA.

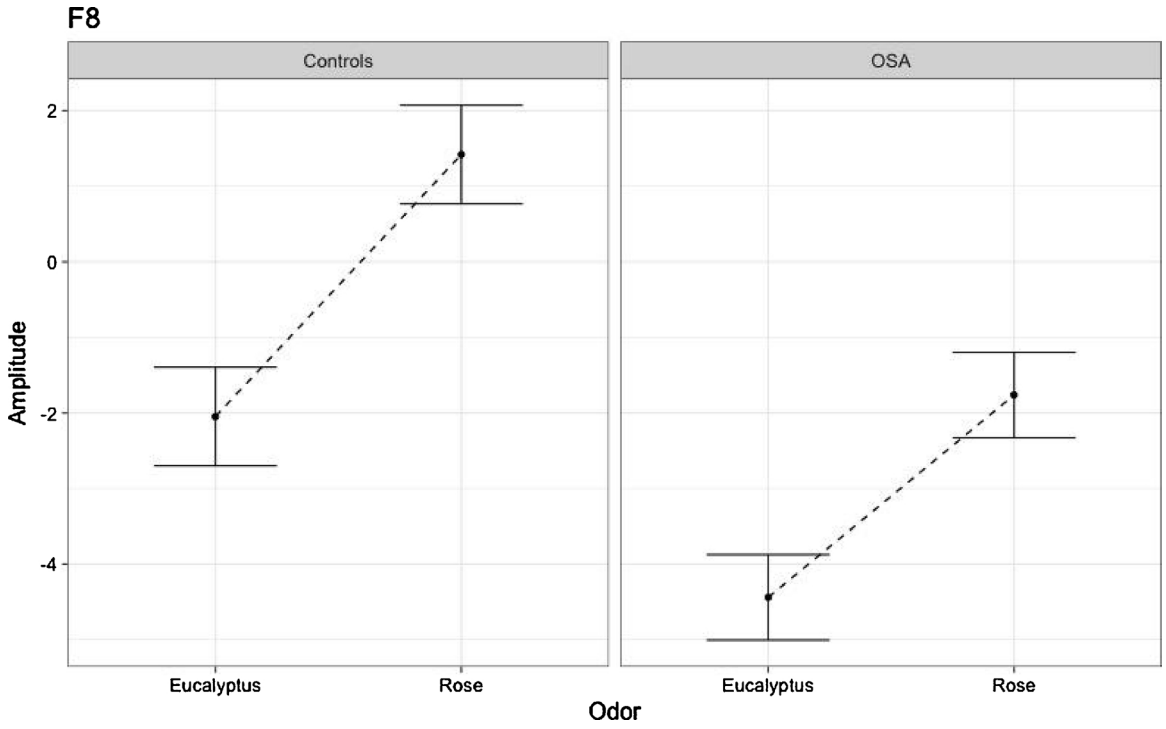


**Fig. 6.** LPC Averaged Amplitude in F8 Electrode in OSA and in Healthy Subjects for Rose and Eucalyptus Smell.

paradigm, the control subjects present ERP component evident for the (rare) target stimulus (i.e., rose) stimulation and a less evident component during the non-target (frequent) stimulus (García-Larrea et al., 1992; Polich and Margala, 1997) (i.e., Eucalyptus). This proportion is maintained in the OSAs (Fig. 5). Furthermore, the OSA group presents, in N1, a delayed latency and an increased amplitude after rose stimulation in right inferior frontal cortex (F8 electrode). This result could be interpreted as a greater arousal perceiving infrequent stimulus (rose) as target. It can be linked to exogenous components of the stimulus (Pause et al., 1996).

In LPC, results showed the same trend highlighted in N1, in right inferior frontal cortex. The interaction between OSA and odorant condition highlighted significant differences in direction of an increased amplitude during rose odorant. According to this task, the activation of the right inferior frontal cortex is implicated in category learning, memory encoding and retrieval (Aron et al., 2004; Bor et al., 2003; Freedman et al., 2001), processes involved in olfactory perception. Furthermore, results in this area are also linked to an activation in right orbitofrontal cortex, that mediates conscious olfactory perception (Li et al., 2010)

The LPC in OSA presented a faster latency in left centroparietal lobe (C3 electrode), that is more aroused when orienting responsivity is increased (Bradley, 2009).

LPC data suggested that the endogenous component in OSA could be affected investigating target stimuli. This situation can be the consequence of the exogenous perceptual difficulty highlighted in N1 results. The increased arousal during the odors breathing could also be related to the attention given to respiratory activity (Gomez et al.,

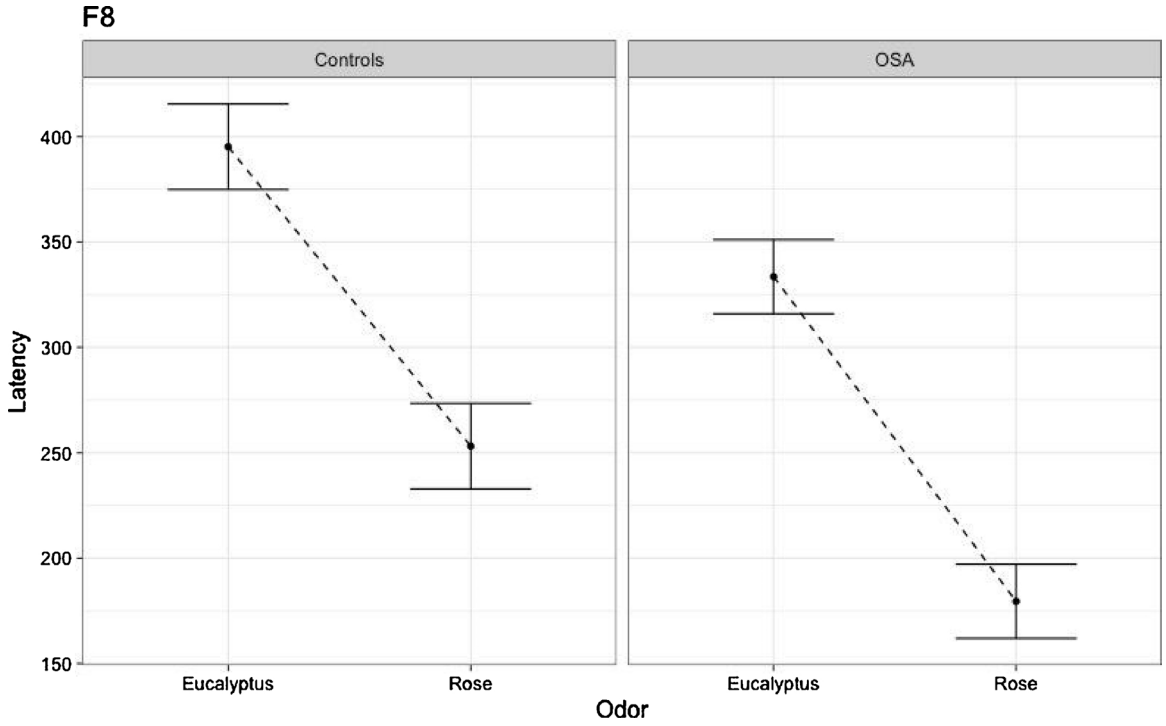


**Fig. 7.** LPC Averaged Latency in F8 Electrode in OSA and in Healthy Subjects for Rose and Eucalyptol Smell.

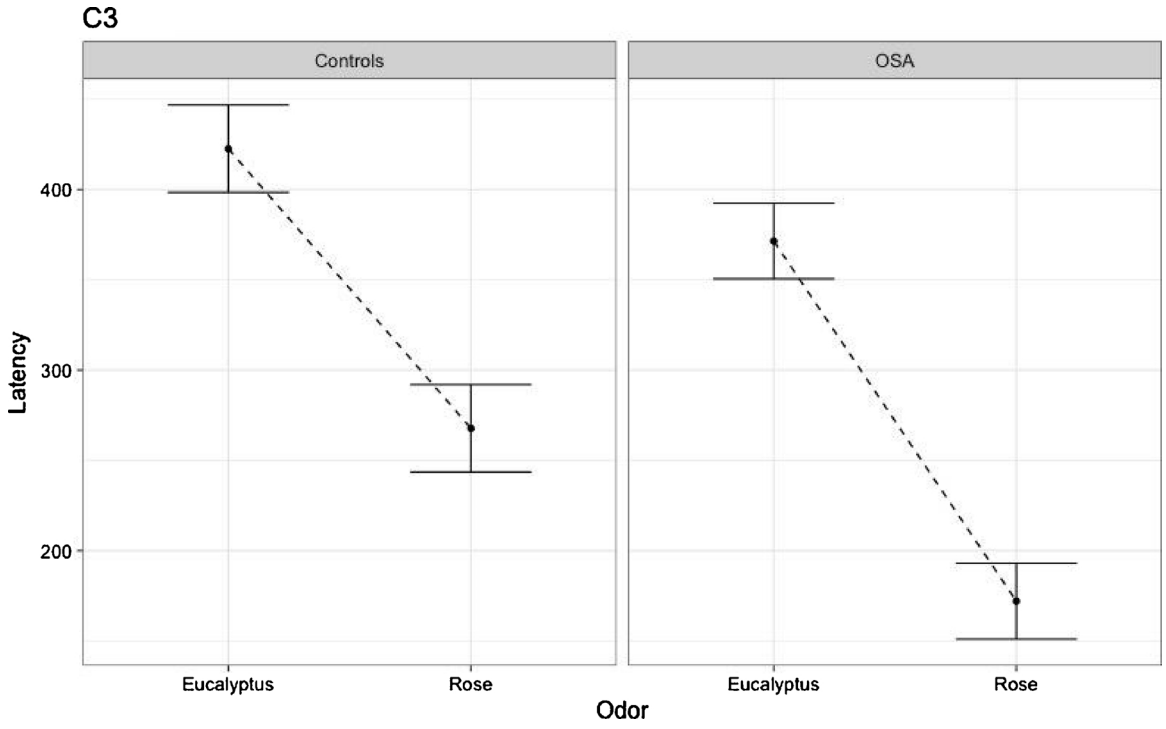


**Fig. 8.** Averaged Latency in C3 Electrode in OSA and in Healthy Subjects for Rose and Eucalyptus Smell.

2008; Yackle et al., 2017) during the smell discrimination.

We also exclude that the CSERP variations are due to alterations caused by daytime sleepiness (i.e., ESS scores) because several studies indicate that in sleep-related breathing disorders, there are no noticeable correlations between ERP components and daytime sleepiness scales (Oken et al., 2006; Sforza and Haba-Rubio, 2006).

Furthermore, our results could indicate that the olfactory alteration may be one of the precursors described in what the literature highlights as comorbidity in the OSA, i.e., a neurodegenerative component. In fact, one of the precursory symptoms of neurodegenerative disorders, also due to oxidative processes induced by bad breathing, is a reduced olfactory capacity (Bradley and Floras, 2009; Lafaille-Magnan et al., 2017). Another consideration of our data could be associated with the relationship between OSA's high BMI scores and the variation of the olfactory discrimination. The different olfactory perception, is associated with a variation of taste (De Araujo et al., 2003; Small et al., 2013), and is accompanied by a fragmentation of sleep states. These aspects can alter feeding behaviors ultimately promoting obesity and

insulin resistance (Poroyko et al., 2016), contributing to the increase of the BMI scores.

In light of these results, subsequent research needs to be aimed at understanding the correlation between OSA intensity, matched with diagnostic evaluations of cognitive and neuropsychological abilities, and olfactory responses due both to endogenous components and to exogenous components: This investigation could be useful to understand the functional process, not only due to overt pathology, but to its developmental phase, to better understand its etiology and its co-morbidity.

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