Impact of temperature on obstructive sleep apnoea in three different climate zones of Europe : data from the European Sleep Apnoea Database (ESADA)

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on behalf of the European Sleep Apnoea Database (ESADA) collaborators

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Abstract

Recent studies indicate that ambient temperature may modulate obstructive sleep apnoea (OSA) severity. However, study results are contradictory warranting more investigation in this field. We analysed 19,293 patients of the European Sleep Apnoea (ESADA) database cohort with restriction to the three predominant climate zones according to the Koeppen-Geiger climate classification: Cfb (warm temperature, fully humid, warm summer), Csa (warm temperature, summer dry, hot summer) and Dfb (snow, fully humid, warm summer). Average outside temperature values were obtained and several hierarchical regression analyses were performed to investigate the impact of temperature on the apnoea/hypopnoea index (AHI), oxygen desaturation index (ODI), time of oxygen saturation < 90% (T90) and minimum oxygen saturation (MinSpO$_2$) after controlling for confounders including age, BMI, gender and air conditioning (A/C) use. AHI and ODI increased with higher temperatures with a standardised coefficient beta (β) of 0.28 for AHI and 0.25 for ODI), while MinSpO$_2$ decreased with β: -0.13 (all results p<0.001). When adjusting for climate zones, the temperature effect was only significant in Cfb (AHI: β=0.11), and Dfb (AHI: β=0.08) (model 1: p<0.001). The presence of A/C (3.9% and 69.3% in Cfab and Csa, respectively) demonstrated only a minor increase in the prediction of the variation (Cfb: AHI: R^2: +0.003; and Csa: AHI: R^2: +0.007, both p<0.001). Our study indicates a limited but consistent influence of environmental temperature on OSA severity and this effect is modulated by climate zones.

Keywords: Sleep related breathing disorders, environment, climate *zone*

Introduction

Sleep related breathing disorders (SRBD) including obstructive sleep apnoea (OSA) are influenced by a plethora of external factors. In recent years, seasonal changes in temperature and air pollution have been included in the list of possible modulators (Rifkin, Long, & Perry, 2018). However, the number of studies investigating the relationship of environmental factors and SRBD is still small and the results are inconsistent: some studies indicate an increase in apnoea/hypopnoea index (AHI) with colder environment (Cassol et al., 2012; Valham, Sahlin, Stenlund, & Franklin, 2012), while others indicate the opposite relationship (Weinreich et al., 2015; Zanobetti et al., 2010). To investigate this phenomenon further, we analysed the potential seasonal effects on OSA by using a large multicentre and multinational cohort: the European Sleep Apnoea Database (ESADA) (Hedner et al., 2011). ESADA includes sleep centres from the Northeast (Turku, Finland) to the Southwest (Lisbon, Portugal) of Europe, allowing a broad investigation of climate and seasonal effects on OSA at the time of diagnosis.

The Köppen–Geiger climate classification (KGCC) is one of the most frequently used climate classification systems. It includes 5 major global climate zones with subdivision according to seasonal precipitations and temperature (Koeppen, 1884).

In this study, we investigated the impact of maximum outdoor temperature and the climate zones on the severity of OSA.

Methods:

European Sleep Apnoea Database (ESADA):

The ESADA cohort is a multicentre and multinational cohort, that has previously been described (Hedner et al., 2011). In short, unselected patients over the age of 18 years referred to the sleep centres of the ESADA group with suspected sleep apnoea are included in the database. Demographic and anthropometric parameters including age, sex, weight, height, and body mass index (BMI), comorbidities and the sleep study results are recorded. Depending on the protocol of each centre, sleep recording is performed using either type I or type II polysomnography (PSG), or type 3 cardio-respiratory polygraphy recording (PG). Coded data are entered and reported via a web-based system and stored in a central database at the University of Gothenburg, Sweden. The study protocol for the ESADA cohort was approved by the local ethics committee in each centre. For the purpose of this study, data from 24 sleep centres of 18 countries were included.

The data of patients with either a PG or PSG study performed between 2007 to 2017 were extracted from the ESADA database.

Climate zones and temperature data

The cohort was grouped according to the Koeppen-Geiger Climate classification which allowed homogenising the participating sleep centres according to main climate, precipitation, and temperature (http://koeppen-geiger.vu-wien.ac.at/, see Fig. 1).

Further investigation was limited to the three climate zones:

Cfb: Warm temperature, fully humid, warm summer. Included study sites: Antwerp, Berlin, Brno, Dublin, Edinburgh, Giessen, Gothenburg, Grenoble, Hamburg, Paris, Prague, Warsaw and Førde (n= 12,516)

Csa: Warm temperature, summer dry, hot summer. Included sites: Alexandropoulis, Athens, Cãceres, Izmir, Lisbon, Palermo and Split (n=4,338)

Dfb: Snow, fully humid, warm summer. Included sites: Klaipeda, Kosice, Turku (n=2,439).
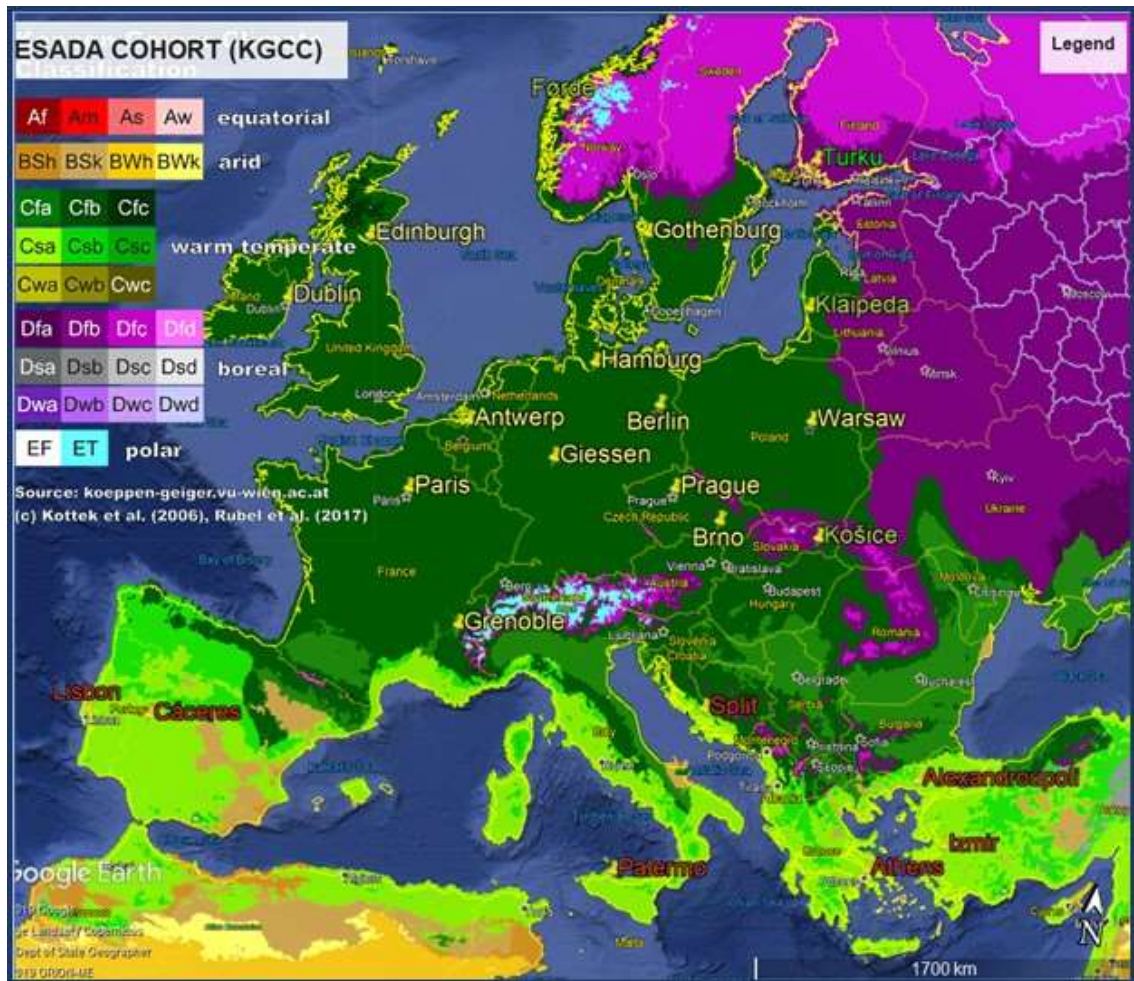
[insert Figure 1 here]

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Figure 1: ESADA cohort according to the Köppen-Geiger Climate Classification. A KMZ file was downloaded from http://koeppen-geiger.vu-wien.ac.at/present.htm and imported into Google Earth with further indication of the participating sleep centres.

Temperature data were obtained with courtesy from the World Bank Climate Databank (World Bank Group Climate Change Knowledge Portal (CCKP): (URL: http://climateknowledgeportal.worldbank.org/). For each sleep centre, the average, maximum and minimum temperature of each month were extracted. Minimum, average, and maximum temperature demonstrated a strong correlation ($r > 0.9$) independently of the climate zone (figure 2). Maximum temperature (MaxTemp) was selected as it might reflect better the possible impact of increasing temperatures in a changing climate.
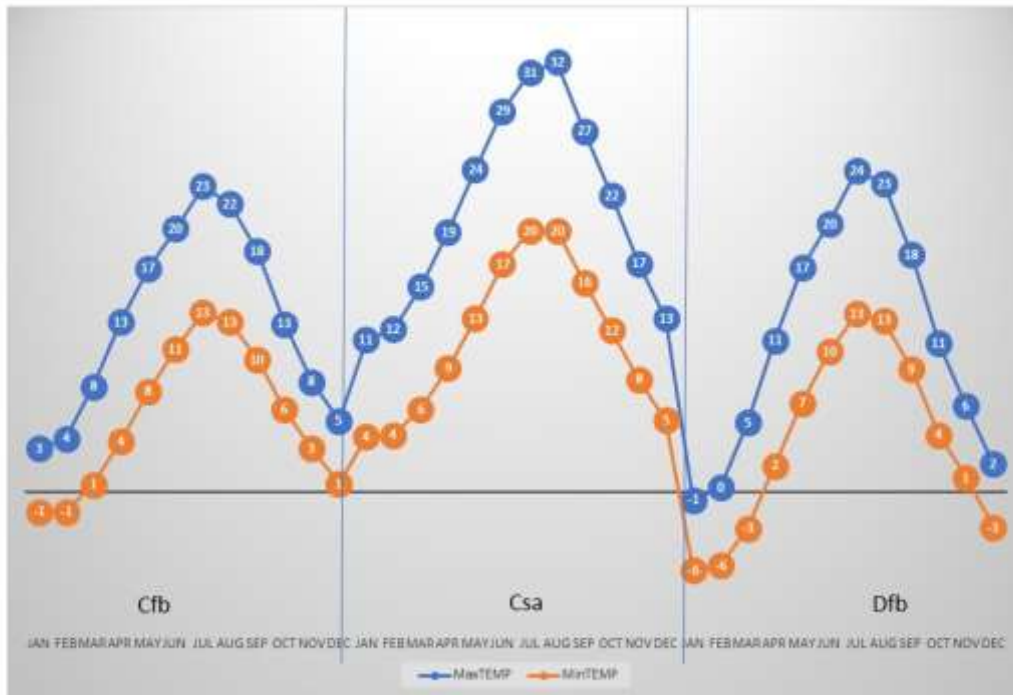
[insert figure 2 here]

Figure 2: Mean values of the annual maximum and minimum temperature recorded in the analysed time period. The Cfb climate zone demonstrated the lowest amplitude between highest temperature in summer and coldest temperature in winter, while Csa showed the highest amplitude

Temperature values were divided into categorical variables with three temperature intervals: low temperature: $\leq 5°$ C, moderate temperature: $>5°$ C to $15°$ C and warm temperature: $> 15°$ C.

Statistical analysis

Descriptive statistics and hypothesis testing were performed using the Statistical Package for Social Science (SPSS) version 24 software (SPSS statistics for windows, Armonk, NY: IBM Corp, USA). Quantitative variables are described as mean and standard deviation (SD). Groups were compared by using one-way analysis of variance (ANOVA) with post-hoc Tukey correction. A significance level of 5% was used to define statistical significance. To analyse the effect size between the groups, Cohen´s D was additionally calculated.

In this study, some respiratory parameters during sleep demonstrated a skewed pattern in the normality analysis and thus did not meet the assumptions for a regression analysis.

After transformation to the natural logarithm (LN) the following variables revealed a normal or almost normal distribution: apnoea/hypopnoea index (LNAHI), oxygen desaturation index (LNODI), the percentage of study time with a peripheral oxygenation saturation < 90% (LNT90). For the minimum oxygen saturation (MinSpO$_2$) we detected a normal distribution without the need for logistic transformation.

We computed a linear regression model to explain the respiratory variables LNAHI, LNODI, LNT90 and MinSpO$_2$ with the 3 temperature intervals controlling for age, BMI, gender, and presence of air conditioning (AC). The same linear regression analysis was repeated with temperature as a linear variable.

The relationship between temperature and the respiratory variables was further investigated by hierarchical block regression analysis. The total model included maximum temperature (block I), age, BMI and gender (block II) and the presence of air conditioning (block III).

Results

A total of 19,293 patients from 24 sleep centres were included in this study. Clinical data are represented in Table 1. The recruitment of participants for each month of the year varied between the three climate zones (see table S1). Although there was a lower recruitment in July for Cfb and in August for Csa the participating sleep centres reported no possible bias such as a preferred selection of clinically severe patients during the period of the summer vacation (see supplemental information). For Dfb we found no clear change in recruitment during the summer months.

Table 1. Baseline data and sleep recording results

[insert table 1 here]

	Total Cohort (n=19293)	**Cfb (n=12516)**	**Csa (n=4338)**	**Dfb (n=2439)**	**P value** 1: Cfb vs. Csa: 2: Cfb vs.Dfb 3: Csa vs. Dfb
Age [years]	52.3±12.6	52.2±12.8	52.7±12.4	52.0±12.1	1: 0.028 2: n.s. 3: n.s.
BMI [kg/m^2]	31.1 ±6.5	30.8±6.3	32.0±6.6	31.6±6.8	1: <0.001 2: <0.001 3: n.s.
Male [%]	70.2	71.0	71.9	63.4	
AHI [/h]	26.8 ±24.7	24.5±23.1	34.1±26.3	25.2±26.8	1: <0.001 2: n.s. 3: <0.001
ODI [/h]	23.1±24.4	21.0±22.8	30.1±26.9	21.±25.2	1: <0.001 2: n.s. 3: <0.001:

T90 [minutes]	39.6±74.8	38.4±75.0	41.8±74.1	38.5±76.2	1: n.s.
					2: n.s.
					3: n.s.
MinSpO$_2$ [%]	80.5±10.0	80.9±9.4	78.7±11.4	81.8±10.0	1: <0.001
					2: =0.001
					3: <0.001
PSG [%]	50.5	41.4	71.1	62.8	

Table 1: Results are displayed as mean values with standard deviation (SD) and percentage for the male sex and the polysomnography parameters. The statistically significance of the post-hoc multiple comparison analysis is displayed in the last column. Abbreviations: AHI: apnoea-hypopnoea index, Cfb: warm temperature, fully humid, warm summer, Csa: warm temperature, summer dry, hot summer, Dfb: snow, fully humid, warm summer. ODI: oxygen desaturation index, T90: time of oxygen saturation < 90 %, MinSpO2: minimum oxygen saturation, PSG=polysomnography.

The ANOVA analysis with post hoc Tukey correction for multiple comparison analysis of the baseline and sleep data revealed for most values small but statistically significant differences between the climate zones (Table 1).

Obstructive sleep apnoea in three different temperature environments

In all four investigated respiratory variables, we detected a highly significant difference between the cold and the warm environment. While LNAHI, LNODI and LNT90 demonstrated an increase with higher temperature, the value of MinSpO$_2$ was significantly reduced. Therefore, the OSA severity increased in the warmer environment with a relevant effect size for LNAHI (d=0.33) and ODI (d=0.29). All results are displayed in figure 3, and table S2. When controlling for age, BMI, and gender results remained statistically significant with LNAHI cold vs. mild temperature reaching a d of 0.05, p<0.001 and cold vs. warm with a d of 0.17, p< 0.001.
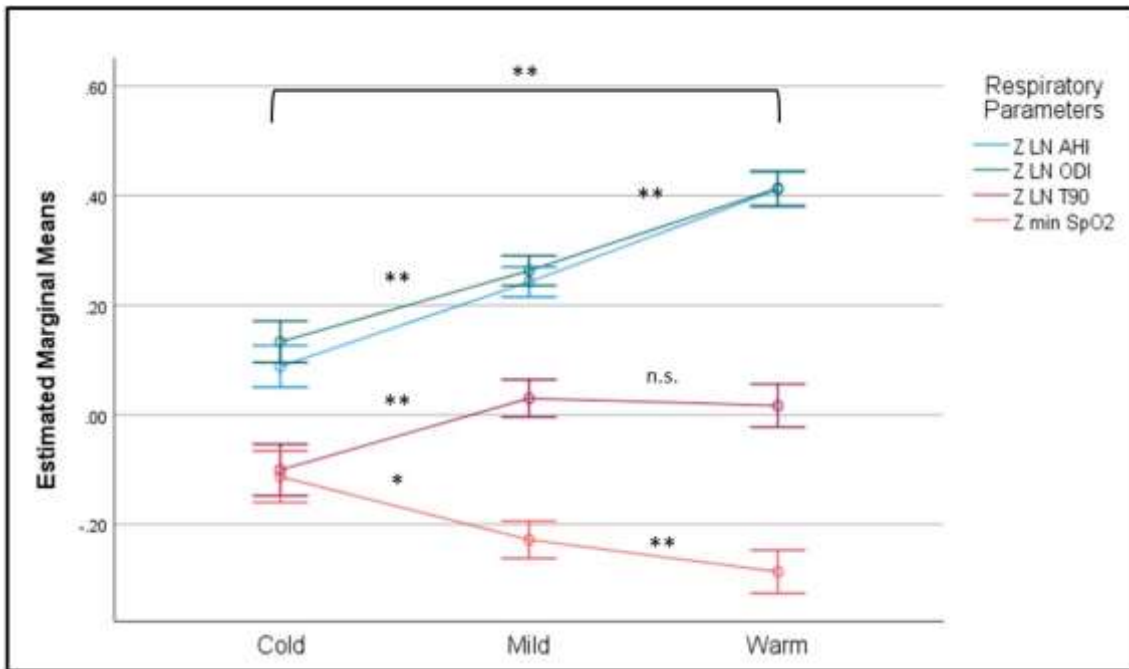
[insert figure 3 here]

Figure 3: Standardised means (Z) with 95% confidence interval depicted as error bars. Between the LNAHI and LNODI we detected a highly correlated linear increase from cold to the warm temperature. For the MinSpO$_2$ the inverse reaction was observed with the lowest values in the warm temperature. T90 increased from cold to mild temperature without further increase in the warm environment. Statistically significant results with $p<0.05$ are indicated by * and with $p<0.001$ by **. In all four respiratory variables we observed highly significant results ($p<0.001$) when comparing cold with warm environment.

Influence of temperature as a continuous variable on OSA severity

The analysis was repeated with maximum temperature (MaxTemp) as independent continuous variable (model 1). The results were controlled for gender, age, and BMI (model 2) and gender, age, BMI and presence of air conditioner (A/C) (model 3).

As shown in table 2, both AHI and ODI increased in higher temperature environments while MinSpO$_2$ demonstrated an inverse direction to higher temperatures. In contrast to this, we found no statistically significant result for T90.

Table 2. Effect of MaxTemp as continuous variable on OSA severity within the total cohort

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[insert table 2 here]

	Model 1		Model 2		Model 3	
	β	P value	β	P value	β	P value
LN AHI	0.28	<0.001	0.24	<0.001	0.25	<0.001
LN ODI	0.25	<0.001	0.22	<0.001	0.21	<0.001
LN T90	0.03	0.051	0.04	0.05	0.03	0.19
MinSpO$_2$	-0.13	<0.001	-0.12	<0.001	-0.11	<0.001

Table 2: Linear regression analysis with the standardised coefficient β of the maximum temperature (MaxTemp) adjusted for age, BMI, gender and presence of air conditioner. Model 1: MaxTemp, model 2: MaxTemp, gender, BMI, age and model 3: MaxTemp, gender, BMI, age, air conditioning. MaxTemp reached statistically significant results for all respiratory parameters except of T90. Abbreviations: LN: natural logarithm, AHI: apnoea-hypopnoea index; ODI: oxygen desaturation index, T90: time of oxygen saturation < 90 %, MinSpO$_2$: Minimum oxygen saturation.

In table 3, the standardised coefficient β (SCB) of all the included variables in model 3 are listed. For all respiratory parameters investigated, BMI revealed the highest values, while the SCB of maximum temperature, gender, and age were almost interchangeable. The presence of air conditioning revealed a small, but statistically significant association.

Table 3. Results from the total cohort. Standardised coefficients β of all variables included in the linear regression analysis model 3.

[insert table 3 here]

	LN AHI		LN ODI		LN T90		MinSpO$_2$	
	β	P value	β	P value	β	P value	β	P value
MaxTemp	0.25	<0.001	0.21	<0.001	0.03	0.194	-0.11	<0.001
Sex	0.24	<0.001	0.22	<0.001	0.13	<0.001	-0.12	<0.001
BMI	0.32	<0.001	0.41	<0.001	0.38	<0.001	-0.41	<0.001
Age	0.25	<0.001	0.26	<0.001	0.21	<0.001	-0.17	<0.001
A/C	-0.03	0.05	0.03	0.097	0.052	0.091	-0.01	0.39

Table 3: Linear regression analysis of model 3 with the standardised coefficient beta (β) of all variables in the equitation. Except for the presence of air conditioner (A/C) all other variables reached statistical significance for LNAHI, LNODI and MinSpO2 value. The correlation coefficient maximal temperature (MaxTemp) did not reach statistical significance in LNT90. Abbreviations: LN: natural logarithm, AHI:

apnoea//hypopnoea index; ODI: oxygen desaturation index, T90: time of oxygen saturation < 90%, MinSpO$_2$: Minimum oxygen saturation.

These results indicate the existence of a small but consistent association between elevated environmental temperature and increases in respiratory parameters during sleep except for T90.

The impact of temperature on respiratory parameters during sleep in different climate zones

Next, we divided the cohort according the Koeppen-Geiger climate classification to investigate the impact of regional climate conditions. A multiple block regression analysis was run for each climate zone of this study. Model I included maximum temperature, model II BMI, Age and gender and for model 3 we added as independent variable the presence of A/C during the sleep study. Main results for LNAHI are shown in table 4.

Table 4. Results from the climate zones: Hierarchical block regression analysis of maximum temperature, BMI and age, gender, and air conditioning on LNAHI

[insert table 4 here]

					MaxTemp	
Cfb	Block	R^2	F change	Significance of F change	Standardised coefficient β	Significance β
	I	0.013	164.31	<0.001	0.11	<0.001
	II	0.233	1173.77	<0.001	0.09	<0.001
	III	0.235	44.99	<0.001	0.09	<0.001
Csa	I	0.000	0,75	0,38	-0.01	0.386
	II	0.194	345.54	<0.001	-0.01	0.335
	III	0.202	39.37	<0.001	-0.02	0.127
Dfb	I	0.006	13.90	<0.001	0.08	<0.001
	II	0.28	291.44	<0.001	0.05	=0.003

Table 4: Results are depictured for the three climates zones Cfb, Csa and Dfb. Block I: maximum temperature, Block II: +age, BMI and gender and Block III + presence of air conditioner. Maximum temperature demonstrated a very small but significant effect in the Cfb and Dfb climate zones while in Csa

there was no effect visible. The impact of air conditioner was small but significant (R^2 change=0.003 in Cfb and 0.007 in Csa). There were no sleep studies with air conditioner in the Dfb climate zones.

Interestingly, we found a modulating effect by the climate zones. While in Cfb and Dfb, the maximum temperature in block I resulted in a small but significant increase of the prediction model, we detected no visible effect for the Csa climate zone. Figure 4 is demonstrating the relationship between maximum temperature and LNAHI for each climate zone with both variables standardised.
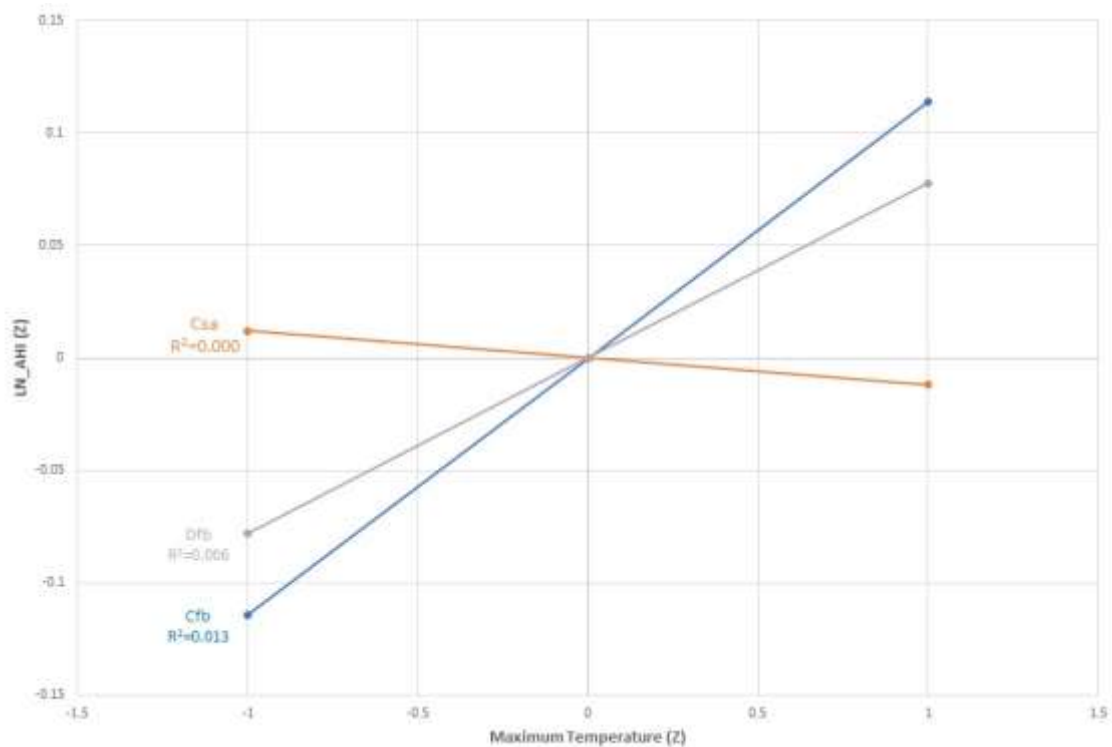
[insert figure 4 here]

Figure 4: Standardised natural logarithm of the apnoea/hypopnoea index (LNAHI) was plotted against standardised maximum temperature values. The Cfb climate zone demonstrated the lowest values of the AHI with a clear temperature dependent increase. This result was also detected in the Dfb climate zone although the effect of temperature was less pronounced compared to Cfb. For the Csa climate zone, we found no relevant effect of the temperature on the LNAHI.

The results for ODI demonstrated an identical pattern (table S3 supplementary material). In clinical terms, temperature might be of interest to interpret the respiratory parameters

during sleep as demonstrated in the simulation in table 6. For a 50-year-old man with an BMI of 28 kg/m^2, the observed temperature surge of 7º C between May and July increased the AHI by 4.21 events /h. Following the temperature reduction of 5ºC in September the AHI decreased for 3.21/h and reached the initial values of May (table 5).

Table 5.

[Insert table 5 here]

(Constant)	1	1	1	1	1	1	1	1	1	1	1	1
MaxTEMP [C]	3.26	4.02	7.91	12.69	16.75	19.68	22.88	21.57	18.01	12.59	8.25	5.34
Gender[m=1]	1	1	1	1	1	1	1	1	1	1	1	1
Age [ys]	50	50	50	50	50	50	50	50	50	50	50	50
BMI [kg/m^2]	28	28	28	28	28	28	28	28	28	28	28	28
LN_AHI [/h]	2.35	2.37	2.44	2.53	2.60	2.65	2.71	2.68	2.62	2.52	2.44	2.39
AHI [/h]	10.57	10.71	11.49	12.52	13.47	14.20	15.04	14.69	13.78	12.50	11.56	10.97

Table 5 Simulation of the relationship between maximum temperature during each month of the year and the AHI. The AHI reflected the evolution of the temperature during the year, resulting in an increase of 4.47 events per hour when lowest temperature in January was compared to highest temperature in July.

The impact of MaxTemp on the MinSpO$_2$ was very small (F change: 23.36), although the result showed high significance ($p<0.001$) in the Cfb climate zone with a negative SCB (-0.05; $p<0.001$ in model 1). Interestingly, in contrast to the LNAHI and LNODI analysis the MaxTemp did reveal a significant increase in the prediction of the MinSpO2 in the Csa group (F change 6.46, $p=0.002$). The SCB was positive with a value of 0.039 ($p=0.01$) in model 1 (table S4).

The effect of MaxTemp on LNT90 was minimal with a R^2 change of 0.001 in the Cfb climate zone. Although the result reached statistical significance ($p=0.009$) its clinical relevance is questionable. In both Csa and Dfb we did not observe a significant effect of MaxTemp on T90.

Effect of air conditioning

Since the measured outdoor temperature does not necessarily reflect the indoor environment at night, we added the presence of A/C to the analysis. The Dfb group was excluded, as no centre of this group indicated any A/C use. While A/C was existing in only 3.9 % of the Cfb climate zone, 69.3% of sleep studies within Csa group were performed in centres with regular A/C use and a high percentage of domestic A/C. Within the total cohort, the standardised coefficient β of A/C did not reach statistical significance (table 3). Nevertheless, it is notable, that although the effect of the air-conditioner was very small, it significantly increased the prediction of the model for all respiratory parameters in both climate zones except for LNT90 in Cfb and MinSpO$_2$ in Csa (supplementary material table S5 and S6).

Discussion

In this large multicentre and multinational observational study, we demonstrated that the seasonal increase of outside temperature results in a small but significant increase in OSA severity. Interestingly, the magnitude of this effect was modulated by climate zones defined by the Koeppen-Geiger climate classification system. Sleep centres belonging to the temperate, oceanic climate (Cfb) revealed the highest response of OSA related severity indices to temperature. In the warm summer and humid continental climate zone (Dfb), the relationship between temperature and OSA values was also present, although not to the same magnitude as in Cfb.

There is a complex relationship between temperature and sleep, since sleep onset itself is linked to a physiological drop in core body temperature (Campbell & Broughton, 1994). An increase in the temperature of the bedroom environment leads to an increase in the number and duration of awakenings during sleep (Karacan, Thornby, Anch, Williams, & Perkins, 1978; Zheng, Li, & Wang, 2019). Recently, Obradovich and colleagues estimated that the predicted climate warming up to 2050 will result in an increase of 6 additional nights of insufficient sleep per 100 individuals (Obradovich, Migliorini, Mednick, & Fowler, 2017). While the importance of adequate bedroom environment for sleep quality has been known for decades, it has only recently been acknowledged that temperature might also influence SRBD.

In 2010, Zanobetti and colleagues were the first to describe the influence of ambient temperature on SRBD. In this cohort based on the Sleep Heart Health Study, a short-term temperature exposure of 25.5º F was associated with an 11.54% increase in the respiratory disturbance index (RDI). The authors postulated that this was due to the direct influence of ambient temperature, but also speculated that this could have been influenced by the seasonal increase in particulate air matter of less than $10\mu m$ (PM_{10}). The PM_{10} during the summer months resulted in a 12.9% increase in the RDI (Zanobetti et al., 2010). While pollutants were not analysed in our study, the results confirm the relevance of increased temperature on respiratory values during sleep. We have been able to demonstrate this using two different models, either with fixed temperature intervals or with temperature as a continuous variable.

In contrast, Valham et al. described a decrease in the AHI when temperature was increased in a sleep laboratory environment (Valham et al., 2012). The results of this study indicate that an increase of 8ºC results in a reduction in the respiratory events during sleep. However, there was no information regarding the participant´s temperature or pollutant exposure during the preceding day. This might be of relevance and will be discussed below since most cross-sectional studies used daytime temperature values and not the values of the bedroom environment.

There are other possible explanations for a seasonal influence on OSA besides temperature alone. Walter and colleagues described an increase in the AHI in children during the winter and spring periods (Walter et al., 2013). The authors interpreted this result in the context of a surge in viral infections during the colder months of the year. Ingram and colleagues investigated the seasonal effect on the frequency of internet research for snoring and apnoea in the United States of America (USA) and Australia (Ingram, Matthews, & Plante, 2015). Results demonstrated a clear increase during the colder months of the year with a magnitude of 5 to 50% in the USA, possibly linked to an increased awareness of these breathing disorders by direct observation. The authors speculated that an increase in body weight and alcohol consumption during the winter holiday season were unlikely to explain this result. This is an important point, since we cannot control either for possible changes in behaviour, e.g. increased consumption of alcoholic beverages during the summer holidays. However, any sleep study performed in-lab will not allow patients to drink excessively, or at all, prior to their test and it is

highly unlikely that this behaviour would be carried over into the home using ambulatory sleep studies.

The result from studies investigating the temperature effects are contradictory so far (Marshall & Cowie, 2015). In a cross-sectional study from Porto Alegre, Brazil, Cassol et al. also described a seasonal impact on sleep apnoea severity (Cassol et al., 2012). Interestingly, although the AHI correlated with temperature, it peaked during wintertime in concordance with results from Valham et al. (Valham et al., 2012; Zanobetti et al., 2010) but in contrast to Zanobetti et al. and our results. In another study from Germany, Weinreich et al. showed that a short-term increase in temperature and ozone was associated with an increase in AHI within the general population (Weinreich et al., 2015). Finally, in a recent single centre study from Taiwan, Cheng and colleagues demonstrated a seasonal effect on OSA with an increase of 2.8 events/h from the summer to the winter periods (Cheng et al., 2019). However, when comparing the larger cohorts, a distinguishing factor can be found. In studies performed in a warmer environment like Porto Alegre, Brazil or Taiwan, the AHI peaked up during the winter period. In the more moderate climate of Germany, AHI was increased during summertime. The fourth study of Zanobetti was also in favour of a worsening of the AHI in the warmer environment, but this study covered several climate zones. Results from the current study were restricted to the three main climate zones within the ESADA cohort. The grouping of sleep centres according to the Koeppen/Geiger climate classification not only homogenised the climate influence, but it also helped to reduce or even exclude the culture influence as possible confounder. In fact, the Cfb climate zone included different countries, like Belgium, the Czech Republic, Germany, Norway, Sweden, and Scotland. Hence, it is surprising that the strongest relationship between temperature and respiratory events during sleep was detected within this inhomogeneous cohort. Distinctive cultural behaviours are therefore unlikely to explain our results.

If elevated temperatures are of any relevance for the respiratory events during sleep, one would assume the clearest results in the regions with the highest temperature, which in our cohort would be the Csa climate zone. However, we were not able to detect a significant effect of ambient temperature on sleep apnoea indices. This lack of difference may be due to the rather stable warm Csa climate without strong drops in temperature as well as the highest use of A/C in sleep centres and homes. Another possible explanation

might be that the population in the South regularly experience hot summer heat waves, which might lead to various adaption processes (Taylor, 2014).

Our study did not systematically capture information on the use of A/C during the in-laboratory or domestic sleep studies. Thus, although there was a significant increase in the prediction when our hierarchical regression model included A/C, its presence or absence was based on generalised information and not confirmed data. One can speculate, that the temperature control of the sleep environment might explain the differences in the study results stated above. Countries with warm climate alike to the Csa climate zone will have frequently temperature control during summer. This applies to work and domestic including bedroom environment. Thus, the possible effect of warmer temperature could be blunted or even reverted in the zones with increased temperature.

Although, the impact of temperature on the respiratory variables was small and possibly with limited clinical impact, we could not confirm its relevance. Our study design did not permit a cause-and-effect analysis and existent pathophysiological data is scarce. For respiratory diseases, an increase of temperature with or without increased air pollutants demonstrated in several studies an increase of respiratory diseases (Zhao et al., 2019) or a worsening of the COPD symptoms (McCormack et al., 2016). Thus, the increased values of the AHI and ODI might reflect a worsening of an underlying respiratory condition. Also, air pollution that is increased with higher temperature demonstrates a negative impact on the oxygen saturation (DeMeo et al., 2004). However, also here the precise mechanism is not yet established and we would expect a more relevant impact of higher temperature on the T90 if lower oxygen saturation was one of the main causes for our observations.

Our results should encourage further studies investigating the effect of the sleep environment, ambient temperature, and air quality on SRBD.

Strengths and limitations of this study

The high number of patients included, and the wide geographical coverage within Europe allows a detailed analysis of the influence of temperature on OSA within three different climate zones. The multicentre/multinational design of ESADA increases the generalisability of our findings. We used various measures of temperature including the minimum, medium and maximum temperature for each month over the analysed time

period. This allows to investigate a generalised influence of temperature but excludes assessment of temperature extremes or a longitudinal approach.

The ESADA cohort is recruited by tertiary sleep centres and any referral bias cannot be excluded. Therefore, the results must be interpreted carefully regarding their applicability for the general population. This study was not designed to contribute to the discussion regarding climate change. Data from the Met Office Hadley Centre published on the homepage of the European Environmental Agency demonstrate a global temperature increase of 0.09º C during the decade of 2007 to 2017 (https://www.eea.europa.eu/data-and-maps/indicators/global-and-european-temperature-9). It is unlikely that this temperature increase during the study would have substantially influenced our results. Also, as stated above, the database does not allow to investigate further outdoor parameters e.g. humidity, or the actual indoor environment.

In conclusion, we showed in this large multicentre, multinational cohort that higher temperatures are associated with an increase in the severity of the apnoea-hypopnoea index, the oxygen desaturation index and the minimum oxygen saturation recorded. There was a clear modulatory effect by climate zones. Any pathophysiological mechanism or causality behind the observed association remains unexplained and needs to be further investigated.

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