New Insights into Weather and Stroke: Influences of Specific Air Masses and Temperature Changes on Stroke Incidence

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Abstract
Background/Objectives: Meteorological factors seem to influence stroke incidence, however, the complex association between weather and stroke remains unclear. Possible explanations from the literature do not categorize into subdivisions of ischemic strokes, only have small patient numbers, or refer to a selection of isolated weather elements without investigating weather changes and more. ***Method:*** In this exploratory trial, almost 18,000 stroke cases from a single stroke center in Southern Germany were analyzed from 2006 to 2015 and classified into the main subgroups of strokes and subdivisions of ischemic stroke etiologies applying the Trial of Org 10172 in Acute Stroke Treatment classification. For each stroke event, the air mass classification was determined from a subset of 7 air mass categories. Relative excess morbidities were derived for the 7 different air mass categories, taking into account the day of the event and up to 2 and 5 days preceding the stroke event. ***Results:*** Statistically significant findings ($\alpha \leq 0.1$) reveal that dry tropical air masses were associated with a lower/higher risk for hemorrhagic (HEM)/macroangiopathic strokes (MAS), respectively. Dry polar air masses were associated with a higher risk for intracerebral bleedings and lower risk for ischemic stroke subtypes. Moist air masses were associated with a reduced incidence of MAS. A strong temperature increase 5 days prior to the event was associated with a lower risk of HEM strokes. Temperature increases were associated with lower risks for MAS and cardio-embolic strokes. Significant temperature decreases were associated with a higher risk of MAS. ***Conclusions:*** Temperature effects were dependent on both air

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masses and temperature changes within 5 days prior to the event and were associated with statistically relevant changes in stroke incidence. Decisive factors such as etiology, age, sex, and risk factors were also taken into account.

Introduction

Fifteen million stroke events are recorded annually by the World Health Organization, leading to disability in many patients and placing a large economic burden on society. In addition to well-established major stroke risk factors, several studies have elucidated the influence of weather elements on stroke incidence [1, 2]; however, the complex association of weather and stroke remains unclear. The inconsistency of the results arises from various factors: such as studying different climate zones, lacking subdivision of ischemic stroke events according to their etiology, small patient numbers, and also a selection bias of stroke centers involved in the studies [1, 3, 4].

The Department of Neurology at the University Hospital Augsburg, Germany, is one of the largest stroke centers in Germany with approximately 1,700 stroke cases per year. This center is solely responsible for stroke patients in the region of approximately 750,000 inhabitants. In collaboration with the Institute of Geography at the University of Augsburg and the Institute of Environmental Medicine of the Helmholtz Society in Munich, we were able to acquire and analyze spatiotemporal variations of climatic determinants for strokes with high resolution.

Air mass classifications are an adequate and well-proven approach for characterizing the weather conditions at a certain location. Air mass classifications consider not only selected individual variables but simultaneously take into account the entire range of relevant weather elements (e.g., air temperature, humidity, cloud cover, wind components, and atmospheric pressure). The benefit of these classifications is that they delineate air masses (weather categories) featuring homogeneous meteorological conditions with respect to the whole set of potentially relevant parameters [5].

Hence, the so called temporal synoptic index approach [6] and the spatial synoptic classification methodology [7, 8] have frequently been used to determine air masses for the investigation of weather-related health effects [9–13], thereby also taking into account potentially health-relevant variations in meteorological conditions over a timeframe of a few days prior to the event [13].

We hypothesized that by addressing the main points of criticism concerning weather and stroke-related studies, this study would give us clear associations between stroke incidence and weather conditions. The points addressed were:

- Reduction of the selection bias by analysis of stroke patient data from a single large stroke center in a geographically well-defined region.
- Analyzing a large number of stroke cases over a long period of time (10 years).
- Subdivision of ischemic strokes according to the "Trial of Org 10172 in Acute Stroke Treatment" (TOAST) criteria [14], including subgroup analyses for age, sex, and classical risk factors.
- Application of an air mass classification rather than using single variables.

Materials and Methods

Identification and Classification of Stroke Patients

Data from almost 18,000 stroke cases were analyzed from our database from 2006 to 2015, and all cases were classified into the main subgroups of strokes, that is, HEM or ischemic strokes, as well as transitory ischemic attacks.

Specific ischemic stroke etiologies were analyzed using the TOAST classification. As the TOAST classification was not completed for all cases during the patients' stay in hospital, the TOAST classification had to be set up retrospectively from patient records.

To set up the classification retrospectively, the medical discharge reports were electronically searched for corresponding keywords indicating ischemic stroke etiology. The program for this was written with the SAS-Software, version 9.4 at the Institute of Environmental Medicine. The TOAST classification was then completed in a step-by-step process:

First, the Medical Informatics Department at the University Hospital Augsburg provided a dataset (csv-file) with all ischemic strokes from January 2006 until October 2016.

Cases where the program did not find a TOAST classification were exported and manually screened by a clinical neurologist. During this process, the list of keywords was expanded and this then increased automated TOAST classification.

To ensure the quality of data throughout the automated TOAST classification: 1% of all the discharge reports were checked manually by a neurologist with regard to the TOAST classification. The result was compared with the automated TOAST classification. In 94% of the cases, the automatic search was the same as the manual classification.

Similar to the TOAST classification, demographic data and confounders as imaging and cerebrovascular risk factors (hypertension, hypercholesterolemia, diabetes, nicotine abuse, obesity, etc.) were extracted by the SAS program. Obesity and nicotine abuse were only registered in 19.1 and 19.3% of all cases, respectively. This, however, we assume is due to a lack of systematic registration of these risk factors in discharge reports rather than the information not being extracted by the SAS program.

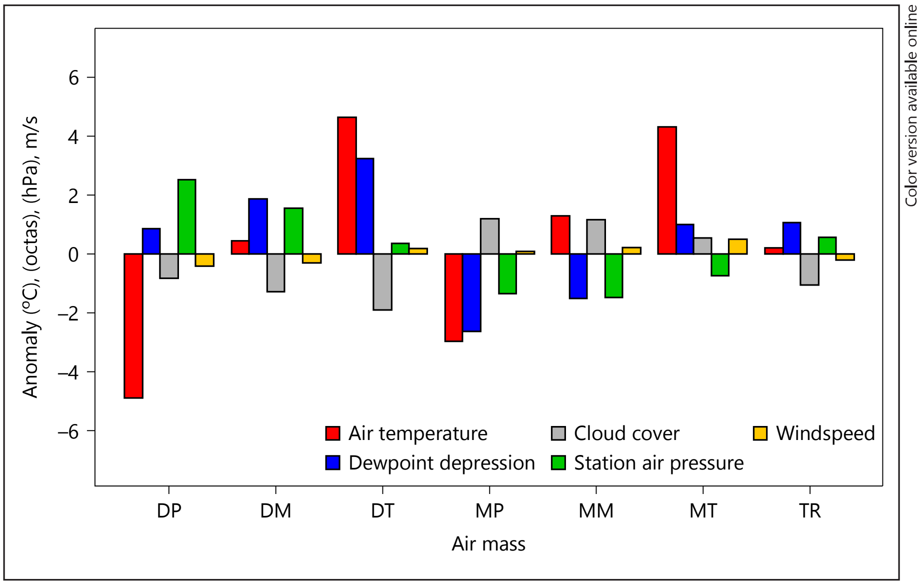

Fig. 1. Mean meteorological anomaly characteristics of the 7 air mass categories for Augsburg in the period 2006–2015. Shown are anomalies – mean differences to the respective monthly mean values – for daily mean air temperature (°C); daily mean atmospheric pressure (hPa); dewpoint depression at 15 UTC (°C); daily mean cloud cover (octas); daily mean wind speed (m/s). DP, dry polar; DM, dry moderate; DT, dry tropical; MP, moist polar; MM, moist moderate; MT, moist tropical; TR, transitional type.

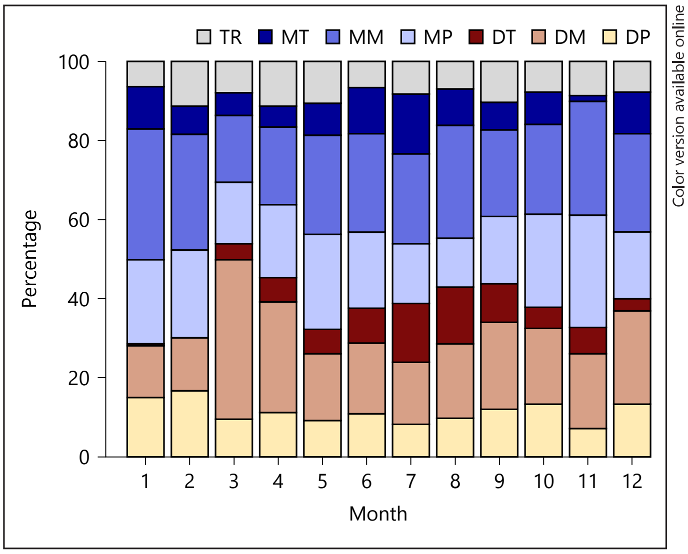

Fig. 2. Monthly relative frequencies of air mass categories in the period 2006–2015. TR, transitional type; MT, moist tropical; MM, moist moderate; MP, moist polar; DT, dry tropical; DM, dry moderate; DP, dry polar.

Meteorological Data Acquisition and Statistical Analysis

Using hourly and daily meteorological data from the official observing station of the Deutscher Wetterdienst at Augsburg-Mühlhausen (DWD 2018) and following the approach documented in Bower et al. [15], an air mass classification for Augsburg was determined by "refining" an initial temporal synoptic index-based classification according to the spatial synoptic classification methodology [16, 17].

This provided a daily calendar of air masses at Augsburg for the period 2006–2015. Seven air mass categories were defined that are characterized particularly through specific thermal and hygric conditions (Fig. 1). These air mass categories also show distinct differences concerning cloud cover, barometric pressure, and wind speed (Fig. 1). Thus, the resulting air masses enable a comprehensive characterization of each day of the analysis period not only considering one specific meteorological element – for example, air temperature – but including a multitude of parameters that together define the weather conditions. In detail, the 7 categories are dry polar (DP), dry moderate, dry tropical (DT), moist polar (MP), moist moderate, moist tropical, and a transitional type (TR) characterized by changeable weather conditions.

Highest/lowest air temperatures are observed for the dry air mass categories DT and DP, respectively. MP and DT feature most the pronounced negative/positive anomalies in dewpoint depression, thus indicating distinctly wet/dry conditions, respectively. A clear and reasonable distinction between moist and dry air mass categories also becomes obvious with respect to cloud cover, barometric pressure and – least pronounced – wind speed (Fig. 1). The most frequently occurring, the thermal moderate air mass categories frequencies, are moist moderate and dry moderate. Remarkably, there was a distinct summer peak with high occurrence of the DT air mass category (Fig. 2).

Our analyses of the relationship between air masses and stroke occurrences in the Augsburg region are based on the average excess morbidities for strokes that are associated to specific air masses.

First, a standardization procedure [18–20] of the daily numbers of stroke occurrences was performed to eliminate the effect of long-term changes (e.g., due to demographic changes) and short-term variations (related to annual and weekly cyclic effects) in stroke morbidity.

Accordingly, the expected number (baseline) of stroke occurrences for each day of the analyzed period Se (y, d) was determined as:

$$Se\,(y, d) = Se\,(d) \cdot WC\,(y, d) \cdot AC\,(y)$$

Where y denotes the year of the analysis period, d denotes the day of the year, Se (d) is the mean morbidity (daily number of stroke occurrences) on day d in a year (computed from the mean annual cycle comprising all years of the analysis period), WC (y, d) is used to correct for any observed weekly cycle in morbidity (calculated separately for individual week-days as the ratio of mean morbidity related to this week-day to the overall mean morbidity), and AC (y) denotes a correction factor for inter-annual changes in morbidity (calculated as the ratio of the number of stroke occurrences in year y to the overall mean annual number).

Daily excess morbidities for each day of the analysis period were then derived from the deviations of the observed stroke occurrences from the baseline data (expected occurrences), and the relevance of specific air-masses for stroke occurrences was estimated by calculation of the respective average excess morbidities. Finally, 2-sided one-sample *t* tests were applied to determine those air masses featuring average excess morbidities that are significantly (for $\alpha = 0.1, 0.05, 0.01$) different from zero and thus represent stroke-relevant weather conditions. The one-sample *t* test assumes normality of the samples but has been shown to be rather robust against non-normality and even in the presence of skewed sample distributions, given a sufficient sample size [21]. However, as the assumption of normality is fulfilled only for a minority of the samples analyzed in this study, complementary non-parametric one-sample Wilcoxon tests were performed to confirm results from parametric tests. For air masses (or air mass sequences as detailed below) occurring on less than 30 days over the entire time period, any rejections of the null hypothesis were not considered and not further interpreted in order to avoid the potential misinterpretation of spurious test results.

To deal with the potential problem of multiplicity due to the large number of pairwise tests, we followed the recommendations for dealing with multiplicity in exploratory studies by Streiner and Norman [22] and refrained from using multiplicity adjustments to not discard potentially interesting effects and chance findings.

In addition to comparing the daily stroke morbidity to the air mass category occurring on the same day (day 0), excess morbidities were also determined for 2-day sequences of air masses prior to day 0 (day –1 and day 0) as well for 5-day sequences prior to day 0 (day –4 to day 0). Taking into consideration the thermal air mass characteristics and in particular respective short-term changes and variations, the 2- and 5-day air mass sequences have been grouped in the following way:

Thermal air mass characteristics have been transformed into numerical values indicating increasing levels of temperature (pola r = 1, moderate = 2, tropical = 3).

Based on these indices, a temperature increase, decrease, persistence (no change in indices) or changeable conditions (air mass TR occurring on at least 1 day) can be deduced for the 2-day sequences.

For the 5-day sequences, temperature indices were averaged for the sequence of days -4 to –2 and for days –1 to 0. Differences between the 2 averages were used to quantify the direction and magnitude of the temperature change over the 5-day sequences (slight increase/decrease: $0.5< = |\text{difference}| <1$; moderate increase/decrease: $1< = |\text{difference}| <1.5$; strong increase/decrease: $1.5< = |\text{difference}|$). If the indices were constant over all the days, persistent temperatures were deduced. Finally, sequences were denoted as changeable if the temperature indices varied each day or if air mass TR occurred on at least 3 days of the 5-day sequence.

The analyses described above were performed separately for HEM and ischemic strokes. Concerning the latter, a further distinction was made for macroangiopathic, microangiopathic, and cardio-embolic subtypes and further distinctions were made for age (under/from 65), biological sex, and the presence/absence of relevant risk factors (smoking, obesity, hypercholesteremia, diabetes, hypertension).

Pseudonymization and Ethical Assessment

Pseudonymization, access and storage are described in detail in the amended data protection protocol. On the basis of the aforementioned protocol with special regard to pseudonymization aspects, the study was approved by the local institutional review board (No. 2016-5, July 19, 2016) and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Results

Patient Characteristics and Stroke Subtypes

Between January 2006 and October 2016, 17,989 cases were analyzed regarding main subgroups of strokes: 1,173 were determined as HEM, 11,875 as ischemic strokes, 4,941 were classified as transitory ischemic attacks.

Main patient characteristics of ischemic stroke patients including sex, age, risk factors, and the distribution of subgroups are displayed in Table 1.

Mean relative excess morbidities for air mass categories and air mass sequences are shown for ischemic and HEM strokes in Figure 3 and for subtypes of ischemic strokes in Figure 4.

Stroke Incidence and Current Weather Conditions

DT air masses were associated with a lower risk of HEM strokes for male patients and no effect could be detected for ischemic strokes on the global scale (Fig. 3). However, DT led to a higher risk for macroangiopathic strokes (MAS; Fig. 4, 5a). This effect was independent of sex and age but only appeared in patients with predisposing risk factors.

In contrast, DP air masses were associated with a higher risk of intracerebral bleedings for patients over the age of 65 years and a reduced risk for all ischemic stroke subtypes for patients >65 years (Fig. 3, 5b). MAS were influenced irrespective of the age groups, whereas cases of CES and microangiopathic strokes (MIS) were only reduced for patients over 65 years of age (Fig. 4). Again, risk factors played a role and the effect was only detectable in patients with cerebrovascular risk factors independent from the sex of the patient.

Moist air masses in general with the exception of MP were associated with a reduced incidence of strokes but the effect was only detectable in MAS. Moist air masses did not show a significantly increased stroke incidence.

The most distinct effects resulted from temperature differences in dry air masses. Therefore, we focused the further analysis on changes in temperature within 2 or 5 days prior to the event.

Table 1. Baseline patient characteristics: p values for statistical connection were calculated with Qui2-tests for each confounder. Regarding age 2 groups were defined: ≥65 years (72.8%) and <65 years (27.2%). The older age group is significantly more represented in all TOAST classes except in strokes of microangiopathic origin. There is a significant relation between hypertension and all TOAST classes except the class "unclear origin." For sex only in strokes of macroangiopathic and CES origin, a significant relationship could be found: more male patients are in the TOAST class of macroangiopathic origin whereas more female patients are in the cardiogenic TOAST section

Patient characteristics	Macroangiopathic (1)		CES (2)		Microangiopathic (3)		Other origin (4)		Unclear origin (5)		Total	
	number	PctN	number	PctN	number	PctN	number	PctN	number	PctN	number	PctN
Gender												
Male	1,587[b]	54.6	1,807[c]	49.0	828	52.6	69	54.3	1,629	53.2	5,920	52.1
Female	1,321	45.4	1,884	51.0	745	47.4	58	45.7	1,435	46.8	5,443	47.9
Age, years												
≤65	745[a]	25.6	895[c]	24.2	457	29.1	66[c]	52.0	933[c]	30.5	3,096	27.2
>65	2,163	74.4	2,796	75.8	1,116	70.9	61	48.0	2,131	69.5	8,267	72.8
Diagnostics*												
Neither MRT nor CCT	80	2.8	94	2.5	41	2.6	1	0.8	89	2.9	305	2.7
MRT	923	31.7	1,023	27.7	534	33.9	47	37.0	1,016	33.2	3,543	31.2
CCT	1,832	63.0	2,456	66.5	965	61.3	75	59.1	1,843	60.2	7,171	63.1
Risk factors												
Hypertension	2,102[a]	72.3	2,528[c]	68.5	1,185[c]	75.3	74[b]	58.3	2,135	69.7	8,024	70.6
Nicotine abuse	599	20.6	538	14.6	320	20.3	27	21.3	611	19.9	2,095	18.4
Hypercholesterolemia	1,277	43.9	1,291	35.0	701	44.6	44	34.6	1,276	41.6	4,589	40.4
Diabetes	728	25.0	742	20.1	408	25.9	24	18.9	638	20.8	2,540	22.4
Obesity	589	20.3	667	18.1	341	21.7	22	17.3	638	20.8	2,257	19.9
Sum of risk factors*												
0	492	16.9	812	22.0	234	14.9	36	28.3	554	18.1	2,128	18.7
1	666	22.9	1,021	27.7	345	21.9	26	20.5	752	24.5	2,810	24.7
2	896	30.8	1,065	28.9	533	33.9	37	29.1	981	32.0	3,512	30.9
3	613	21.1	588	15.9	320	20.3	22	17.3	555	18.1	2,098	18.5
4	207	7.1	174	4.7	121	7.7	5	3.9	191	6.2	698	6.1
5	34	1.2	31	0.8	20	1.3	1	0.8	31	1.0	117	1.0
Sum	2,908	25.6	3,691	32.5	1,573	13.8	127	1.1	3,064	27.0	11,363	100.0

[a] $p < 0.05$.
[b] $p < 0.01$.
[c] $p < 0.001$.
* No p values calculated.
CES, cardiogenic; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Analysis of Stroke Incidence and 2-Day Sequences

Two-day sequences did not reveal many pronounced effects on the incidence of strokes, independent on whether they were ischemic and HEM strokes or ischemic stroke subtypes. Only 2 observations with an increased temperature were found: First, leading to a reduction of MAS but only for patients <65 years and secondly a temperature decrease associated with a reduction of stroke incidence for patients >65 years.

Analysis of Stroke Incidence and 5-Day Sequences

Only in male patients a strong temperature increase was associated with a lower risk of HEM strokes, whereas a slight decrease in temperature had the opposite effect (Fig. 3). Air masses and temperature changes had no significant effect on bleedings in female patients.

Temperature increases were associated with lower risks for MAS and CES (Fig. 4, 5c), however, a strong temperature increase was associated with an increased risk for CES. This effect was independent of the sex in both subgroups whereas the CES risk was only reduced in the group with risk factors. There was no significant effect in younger patients for MAS and CES. Interestingly, temperature increases only reduced the risk of MIS in younger patients without a significant signal in the other groups.

Strong temperature decreases were associated with a higher risk of MAS (Fig. 5d), especially for male and older patients with risk factors whereas strong temperature decreases can be attributed to reduced CES in male patients and reduced MIS in younger patients without risk factors.

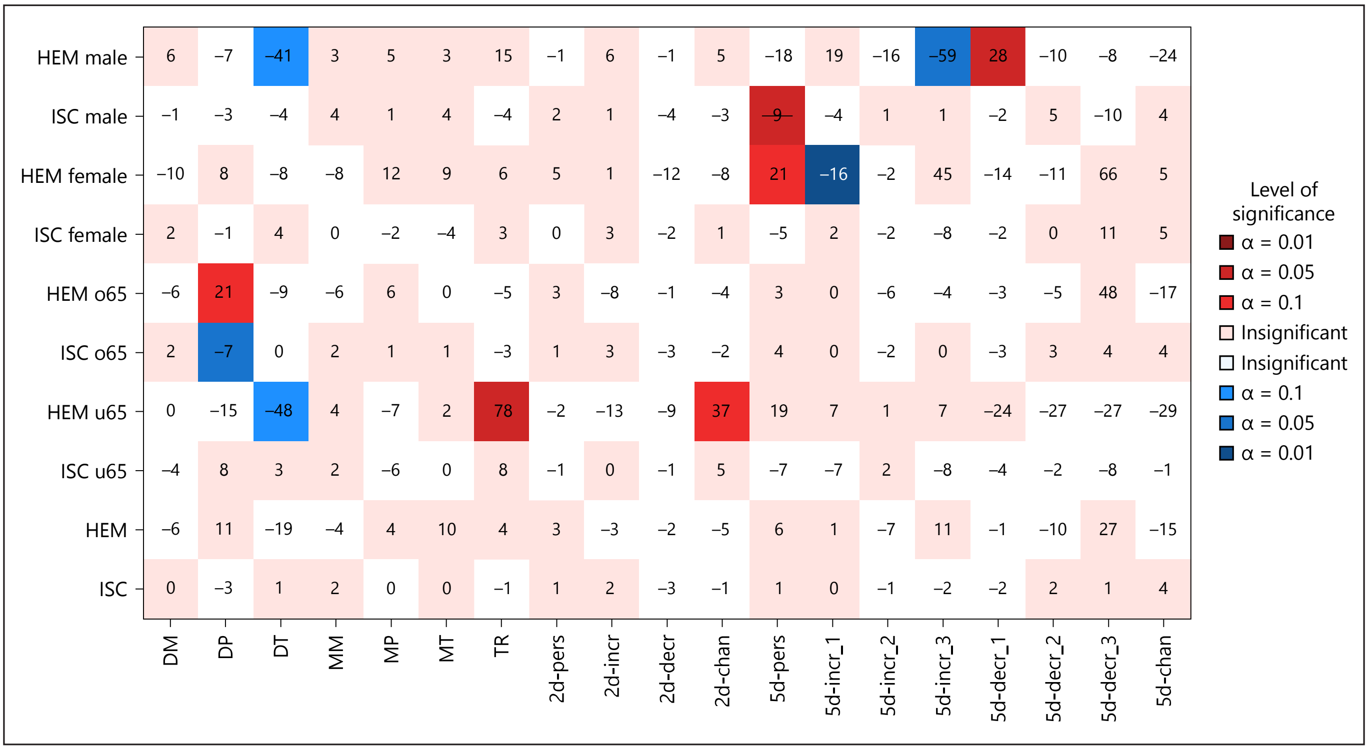

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Fig. 3. Mean relative excess morbidities (in %) of air mass categories and air mass sequences for ischemic and HEM strokes. Air mass sequences along the x-axis include 2-day sequences featuring persistent (2d-pers), changeable (2d-chan), increasing (2d-incr), and decreasing (2d-decr) temperature characteristics; 5-day sequences include persistent (5d-pers), changeable (5d-chan) and slight, moderate and strong increasing/decreasing temperature characteristics (5d-incr_1–3, 5d-decr_1–3). See text for further explanation of categories of air masses and air mass sequences. Abbreviations along the y-axis ISC and HEM strokes and subgroups (u65/o65 – age under 65/above 65; female/male). Light shaded colors indicate insignificant mean relative excess morbidities, with red and blue indicating positive/negative sign, respectively. Darker shaded red and blue colors indicate significant mean relative excess morbidities (for α = 0.1, 0.05, 0.01) according to a one-sample *t* test. Strikethrough numbers denote results that could not be confirmed by a non-parametric Wilcoxon test (at least for α = 0.1). DM, dry moderate; DP, dry polar; DT, dry tropical; MM, moist moderate; MP, moist polar; MT, moist tropical; TR, transitional type; HEM, hemorrhagic; ISC, ischemic.

Discussion

Using a large number of stroke cases during a period of nearly 10 years, we were able to find an association of dry air masses with the incidence of HEM and ischemic strokes: higher temperatures in dry weather conditions led to a lower risk of intracerebral hemorrhages (ICHs) and a higher risk of MAS. The opposite effect could be observed with low temperatures in this study. This effect on HEM strokes supports findings of a Korean study having observed a negative correlation between ICHs and mean temperature [23]. It also extends previous findings from a study conducted in Finland, which demonstrated a peak incidence of ischemic and HEM strokes in autumn, whereas the lowest stroke incidence was observed in summer [24]. Both of these studies, however, only dealt with single weather elements and do not provide an observation of complex air masses.

The overall risk of ischemic strokes was only slightly affected by lower temperatures, but the sub differentiation of all ischemic stroke subtypes revealed a pronounced effect on the reduction of MAS. MIS were, although represented in a relevant and – according to the literature – plausible proportion [25], not decisively influenced by atmospheric factors. Interestingly, higher daily temperatures were only associated with an increased rate of MIS in a Scottish study [26], a discrepancy, that cannot be explained easily.

As suggested by other studies, another major aspect in understanding the influence of weather conditions on stroke risk are changes in ambient variables in addition to present conditions [27]. Our analysis revealed conclusive effects within 5 days before the index event, which

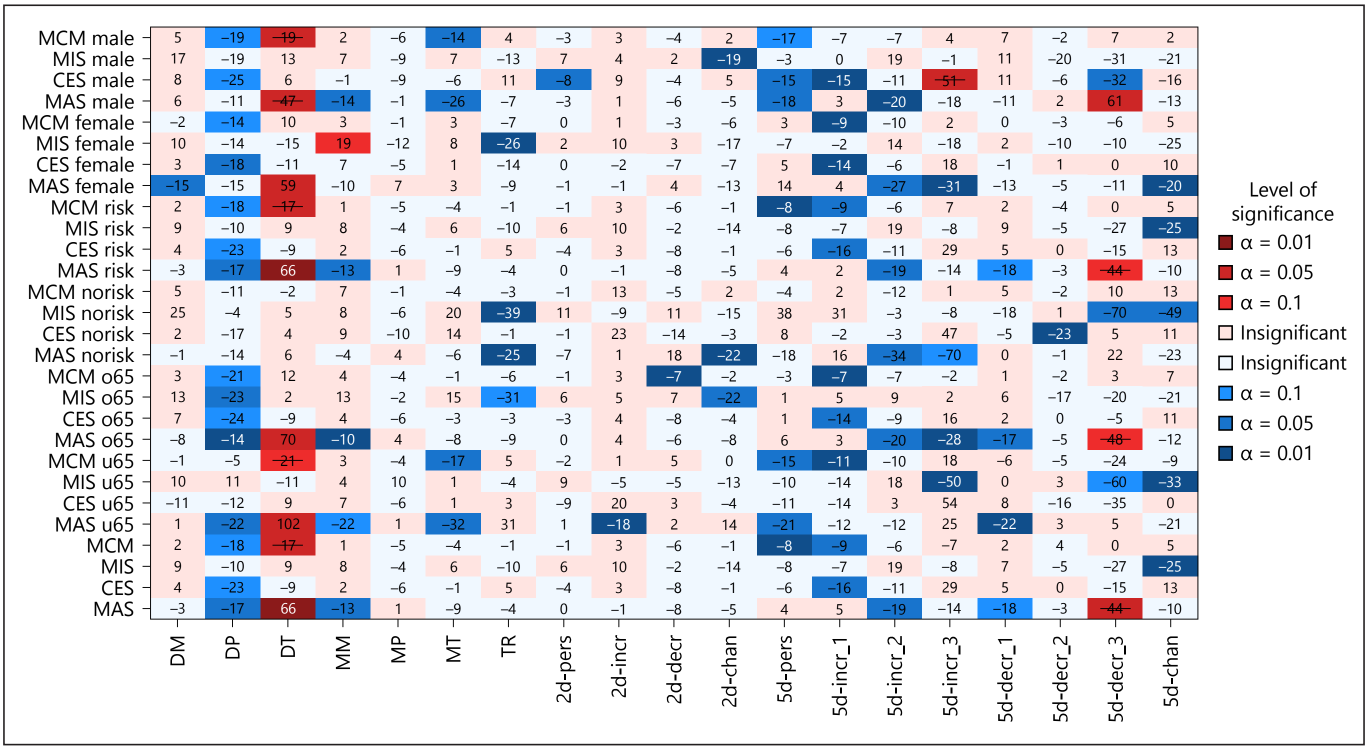

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Fig. 4. Mean relative excess morbidities (in %) of air mass categories and air mass sequences for subgroups of ischemic strokes. Air mass sequences along the x-axis include 2-day sequences featuring persistent (2d-pers), changeable (2d-chan), increasing (2d-incr), and decreasing (2d-decr) temperature characteristics; 5-day sequences include persistent (5d-pers), changeable (5d-chan) and slight, moderate and strong increasing/decreasing temperature characteristics (5d-incr_1–3, 5d-decr_1–3). See text for further explanation of categories of air masses and air mass sequences. Abbreviations along the y-axis indicate combinations of stroke subtypes (MAS; CES; MIS; MCM – MAS, CES, MIS) and subgroups (u65/o65 – age under 65/above 65; no risk/risk – no risk factors/risk factors; female/male). Light shaded colors indicate insignificant mean relative excess morbidities, with red and blue indicating positive/negative sign respectively. Darker shaded red and blue colors indicate significant mean relative excess morbidities (for α = 0.1, 0.05, 0.01) according to a one-sample *t* test. Strikethrough numbers denote results that could not be confirmed by a nonparametric Wilcoxon-test (at least for α = 0.1). DP, dry polar; DM, dry moderate; DT, dry tropical; MP, moist polar; MM, moist moderate; MT, moist tropical; TR, transitional type; MIS, microangiopathic strokes; CES, cardiogenic; MAS, macroangiopathic strokes.

were not recognizable within a 2-day period: only for male patients, temperature changes influenced the risk of ICHs, with an increase in temperature having a protective effect. Temperature increases of all magnitudes were associated with a lower risk of macroangiopathic and cardioembolic strokes, whereas decreases in temperature enhanced the risk of MAS. Rakers et al. [28] were able to show a close to linear association with temperature decreases within 24 h before the index event and a higher risk of ischemic strokes, especially affecting cardioembolic strokes. In our study this effect was reproducible, but temperature decreases were only relevant in a period of 5 days prior to the event and only affected MAS. Pathophysiologically, the predominance of MAS can well be explained by increased blood pressure, peripheral vasoconstriction, increased platelet count, and increased blood viscosity caused by cold weather conditions [29]. All these factors predominantly favor plaque instability or rupture.

We were able to prove that the consideration of age, sex, and the presence of relevant risk factors was decisive for the reaction to atmospheric influences: for example, the risk of ICBs was only reduced for male patients under DT conditions and the influence of temperature decreases on MAS incidence was only relevant for male patients >65 years with relevant risk factors.

At first glance, there seems to be a "thermal paradox" with high temperatures at the time of the event and temperature decreases within 5 days prior to it, both leading to increased incidences of MAS. In a recently published review, Lavados et al. [29] summarize the proposed mechanisms of ambient temperature on stroke incidence. In-

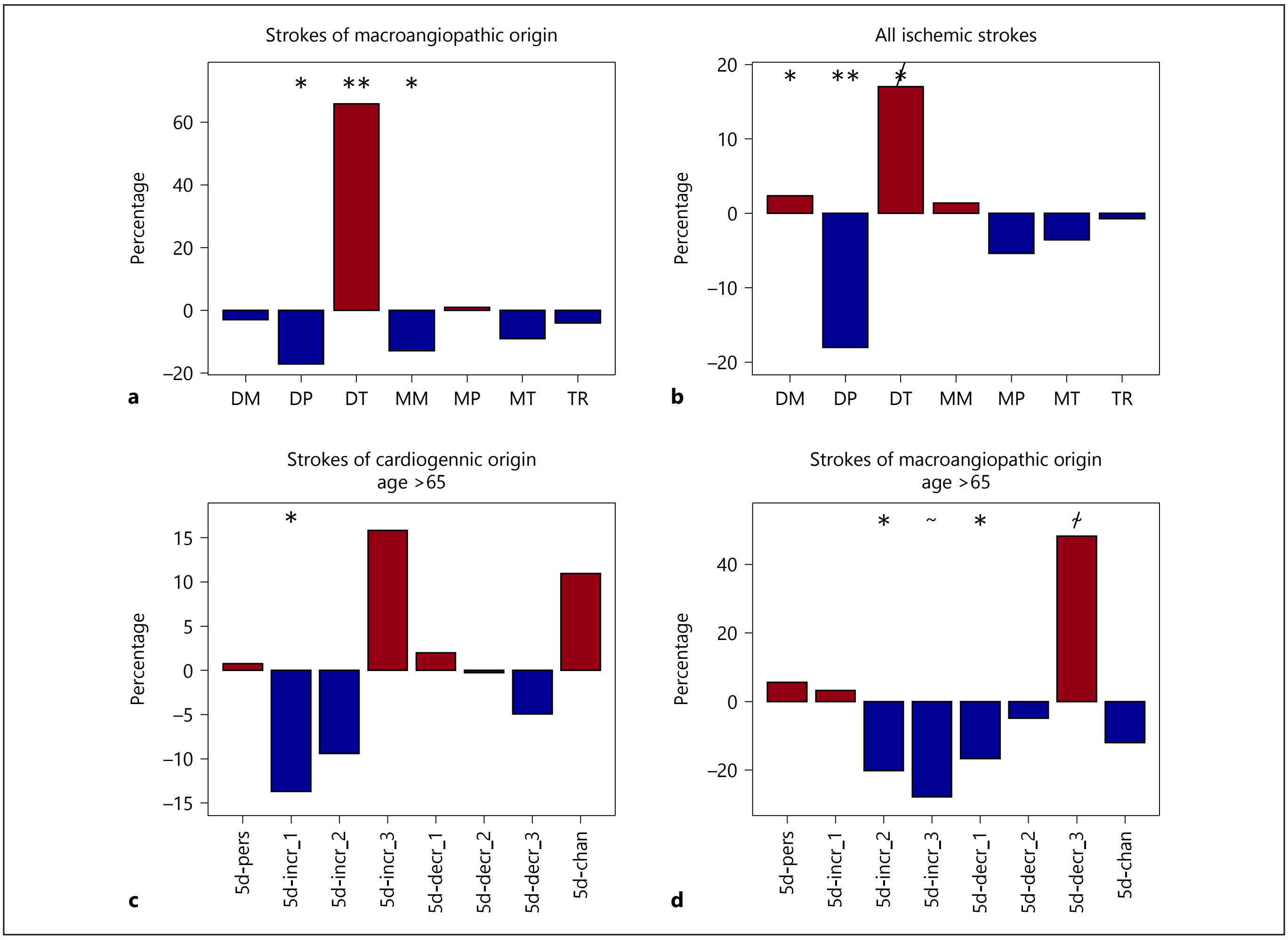

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Fig. 5. Bar plot diagrams of mean relative excess morbidities (in %) of air mass categories and air mass sequences for selected subgroups of ischemic strokes. x axis (**a**, **b**) Air mass categories: See text for further explanation of categories of air masses; (**c**, **d**) Air mass sequences (5-days) include persistent (5d-pers), changeable (5d-chan) and slight, moderate and strong increasing/decreasing temperature characteristics (5d-incr_1–3, 5d-decr_1–3). y axis: mean relative excess morbidities (in %). Level of significance (α): ~ 0.1, * 0.05, ** 0.01 of one-sample *t* tests. Strikethrough symbols denote results that could not be confirmed by a non-parametric Wilcoxon-test (at least for α = 0.1). DP, dry polar; DM, dry moderate; DT, dry tropical; MP, moist polar; MM, moist moderate; MT, moist tropical, TR, transitional type; CES, cardiogenic; MAS, macroangiopathic strokes.

terestingly, either high or low temperatures can elevate stroke risk on the basis of different mechanisms: cold weather leads to raised blood pressure via the sympathetic and the renin angiotensin system whereas higher temperatures lead to increased blood viscosity due to increased urination [29]. Based on our findings, we propose that embolic strokes, especially those triggered by macroangiopathy and MIS differ in that MAS are more acutely influenced by external factors leading to changes of blood pressure, blood viscosity, and inflammation. In contrast, the inflammatory degeneration of small arterioles seems to be a more chronic process.

In our study, we could specify that particular air masses rather than distinct seasons and single weather elements are responsible for changes in stroke risks as the influence of temperature, for example, was only significant in dry weather conditions. This underlines the relevance and usefulness of the air mass concept to understand the influence of weather on cerebrovascular diseases. To the best of our knowledge, this is the first study to have analyzed the influences of complex air masses on stroke incidence and might explain many controversies of temperature effects in other studies.

The determined air masses reflect meteorological conditions representative for a region rather than for a specific location. Hence, the relevance of our results is not confined to the specific study location. However, application of our approach to a region with significantly different climatic characteristics would probably result in the determination of air masses with divergent climatic features and thus also modified significance for stroke risk.

Our study has several strengths: the subdivision of ischemic stroke etiologies, large patient numbers, and a long period of investigation comprising nearly 18,000 stroke cases over approximately 10 years with additional subgroup analyses of ischemic strokes concerning sex, age, and risk factors. Patient data were collected from a stand-alone stroke care provider, minimizing the risk of selection and inclusion bias.

We were able to prove that especially changes in air masses were associated with different stroke risks and that consideration of multiple aspects in stroke etiology, further sub differentiation, and risk factors are decisive for the quality and interpretation of the results.

We also acknowledge that our study has limitations: We were faced with unavoidable problems of any retrospective analyses, as important parts of information possibly noteworthy for correlation with environmental factors were not listed in standard patient discharge documents, defining the need for prospective recording, for example, in a stroke registry setting. The strength of a single-center study to reduce a potential bias of selection and inclusion is necessarily also a disadvantage with regard to the limited number of cases in comparison to multi-center observations.

Summary

Weather seems to be a relevant risk factor for both HEM and ischemic strokes, especially for patients with "classical" risk factors. One important point concerning our data is an obvious correlation between individual risk factors and stroke incidence: our data suggest that in some weather constellations there is a significant association to stroke incidence only for patients with predisposing risk factors. Thus, it seems to be of special relevance when studying the connection between weather and stroke incidence to subdivide stroke cases according to their etiology, sex, age, and classical risk factors. Being confronted with ongoing climate change, more research is needed to ensure that healthcare systems can anticipate conditions of a presumably higher stroke incidence in the future.

These results encourage to further refine and to develop optimized classification-approaches to identify even more precise relationships between specific weather conditions and regional stroke incidence rates. Such substantially advanced classification approaches will explicitly consider sudden weather changes and will additionally take into account not only local but also synoptic scale meteorological and further relevant non-climatic environmental variables like for example, air quality parameters.

Statement of Ethics

The study protocol has been approved by the research institute's committee on human research. The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

M.E. and C.B.: drafting the work, substantial contributions to the conception and design of the work and the acquisition, analysis and interpretation of data for the work. B.K., G.H., A.S., E.G., S.S., and A.P.: acquisition and analysis of data for the work. J. H.: drafting the work, analysis and interpretation of data for the work. C.T.-H. and J.S.: critical revision of intellectual content of the work. J.J. and M.N.: substantial contributions to the conception and design, analysis and interpretation of data, critical revision of intellectual content. All authors finally approved the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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