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ORIGINAL RESEARCH

Essential oils, asthma, thunderstorms, and plant gases: a prospective study of respiratory response to ambient biogenic volatile organic compounds (BVOCs)

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Purpose: Prevailing opinion is that wind-pollinated plants affect asthma negatively and that insect- pollinated ones do not. "Thunderstorm" asthma, too, is attributed to bursting grass pollens. Additional biogenic volatile organic compounds (BVOCs) are identified here. Essential oils' BVOCs are inhaled from plants, oil diffusers, candles, room "fresheners", perfumes, and hygiene products. Claims of BVOC "safety" for sensitive respiratory systems are questioned.

Methods: Fourteen volunteers, of mixed-age and gender, with seasonal asthma recorded peak expiratory flow (PEF) and 11 symptom scores. BVOCs were collected on Tenax tubes from ambient air in autumn and spring, as were live flower emissions, before and after a thunderstorm. Gas chromatography–mass spectrometry analysis identified frequently occurring BVOCs. Air spora, meteorological, outdoor air pollution variables, and BVOCs predict respiratory symptoms in univariate linear regression models, seasonally.

Results: Increased pinene, camphor, linalool, linalyl acetate, benzaldehyde, and benzoic acid predict respiratory symptoms, including reduced PEF, and increased nasal congestion; day length, atmospheric pressure and temperature predict symptoms in both seasons, differently; other variables predict a range of symptoms ($0.0001 \leq p \leq 0.05$). Thunder predicts different BVOC emissions in spring, compared to autumn ($p \leq 0.05$). An uncut *Grevillea* flower emitted linalool and hexenal before a storm; the latter is also emitted from cut grass. Increased nitrogen oxides and pinene in autumn may combine to form harmful oxidation products.

Conclusion: This research supports BVOCs as contributors to seasonal asthma and allergic rhinitis, and "thunderstorm" asthma. Pinene emissions from Myrtaceae species (*Eucalyptus, Melaleuca, Leptospermum, Callistemon*), Brassicaceae (canola), and conifers, worldwide, may induce respiratory inflammation and maintain it, by inhibiting eosinophilic apoptosis. Widely used essential oil products containing BVOCs, like linalool, are associated here with respiratory symptoms. Lagged responses suggest that users' cognitive associations between exposure and response are unlikely, increasing potential for impaired health for vulnerable children.

Keywords: asthma, allergic rhinitis, BVOC, terpenes, *Eucalyptus*, essential oils

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Introduction

Essential oils, consisting of terpenes,[1] and fragrant components are emitted from aerial parts of plants to communicate with pollinators and predators.[2] They are

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widely used in hygiene and lifestyle products[3–5] like essential oil diffusers, candles, room "fresheners", cleansers, perfumes, soaps, shower gels, and deodorants and may be a source of sensitivity[6] and asthma.[7] Asthma affects more than 334 million people worldwide, and its prevalence in the United Kingdom, Australia, New Zealand, Canada, and the United States of America (USA) is notable,[8] but adequate explanations of world patterns remain elusive. Australian causes of asthma have been unclear too, despite a prevalence of 10.8%, one in nine, over 2.5 million people;[9] one in five Australians experiences allergic rhinitis, nearly 4.5 million people.[10] This research investigates respiratory effects of biogenic volatile organic compounds (BVOCs) from Australasian plants, shared by canola, conifers, and other plants, globally.

In late spring 2016, within 30 hrs of a thunderstorm in Melbourne, Australia, there were 3365 (672%) excess respiratory-related presentations to emergency departments, and 476 (992%) excess asthma-related admissions to hospital, and 10 people died.[11] This was attributed to the accepted explanation, that is, inhalation of burst pollen grains that release cytoplasmic granules.[12] Likely additional contributors, BVOCs, are identified here, and results from floral BVOC emissions before and after a thunderstorm are presented.

Asthma prevalence varies, and Queensland's rate is higher than other states at 11.8%.[13] A high level of asthma morbidity has been noted over several decades in South-East Queensland (SEQ) especially in autumn[14] and slightly less in spring.[15] While thunderstorms and their effect upon pollens and fungi explain some spring and summer asthma in SEQ, they are scarce in the cooler and drier autumn peak of asthma symptoms. This is when vast numbers of Myrtaceae family member *Melaleuca quinquenervia (M. quinquenervia)* flower; it is often called "bottlebrush" (Figure 1). Large tracts of *M. quinquenervia*, introduced from Australia, have naturalized in Florida, USA. Considered a pest, it thrives,[16] and has been controversial regarding its possible source of irritancy and respiratory disease.[17]

The focus in Australia,[18–20] and elsewhere,[21] regarding plant-associated asthma, has been anemophilous pollen (wind disseminated), especially grasses and weed pollens. Oil-bearing plants, especially from the Myrtaceae family, containing terpenoids and aromatic compounds blanket the Australasian landscape and have entomophilous (insect-pollinated) pollens that are oily, sticky, and clump together, reducing numbers in pollen traps.

Figure 1 *Melaleuca quinquenervia.*

Myrtaceae family species are championed as safe garden plants for those with allergies and asthma,[22,23] but evidence is lacking. Contrary evidence involves children in SEQ with asthma, who were compared to those without symptoms, in responses to skin-prick tests with 15 allergens.[24] Response to *Eucalyptus* pollen ("gum" tree) was 31 times greater for children with asthma, a difference greater than any other allergen.

Plant emissions

Emission of volatile compounds depends upon the rate of biosynthesis, rate of release,[25] growth stage,[26] daily emission cycles,[27] temperature,[28] light intensity,[28] and vapor pressure[29] within plant tissues. Emission changes may be relevant in "thunderstorm" asthma, when atmospheric pressure reduces, and may increase floral emissions.[30]

Previous time-series research regarding gaseous emissions from plants is scarce. Influential work concerns canola, *Brassica napus*. This cultivar of rapeseed or oilseed rape (OSR) is grown extensively in Australia, Canada, Scotland, the USA, and many other countries and may contribute to asthma there. Emissions of sabinene, alpha-pinene, limonene, delta-3-carene, benzaldehyde, and linalool vary over a growing season.[31] Familiar conifers like pine, spruce, birch, juniper, and cypress, that forest the temperate and cooler parts of the world, also produce these terpenes,[32] as do many other plants.[33] Also found in the oils of the Australian Myrtaceae family plants, they vary in bioactivity[33] and are related to inflammatory response.[1]

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Sensitizing processes

Linalool and linalyl acetate, found in fragrance products, are common sensitizers[34–36] and are components of Myrtaceae leaf oil that oxidize readily. Oxidation makes a terpene more sensitizing,[1,37] for example, limonene,[38] that is used in household cleansers for its lemon scent.[39] Aliphatic aldehydes (eg hexenal, from cut grass, and citral, the lemon scent in lemongrass) and the aromatic aldehydes (eg benzaldehyde) are common in nature;[33] they feature in domestic products and are variously sensitizing.[40] Camphor, a well-known bicyclic ketone found in plants, is used domestically and industrially and is very toxic.[41] Polya[33] identifies thousands of biochemical targets of bioactive terpenes in essential oils and many autoxidize.[34]

Objective

The objective here is exploration of the contribution of plant emissions to symptoms associated with asthma and allergic rhinitis in participants from a coastal location with consistently high levels of seasonal asthma. Air spora, air pollutants, and meteorological variables are measured as well as floral response to a thunderstorm.

Prospective studies investigating the effects of ambient plant-related BVOC's, upon human respiratory processes, are not evident in the literature. This research enhances understanding of respiratory effects of plant gases and domestic usage of essential oil products and urban landscaping choices; it supports the premise that some plant gases contribute to respiratory symptoms.

Methods

Location

Rothwell, part of Redcliffe City, population 55,000, is an outer northern suburb of the Queensland state capital, Brisbane; it is 960 km north of Sydney, Australia. At sea level and coast, it features street plantings of bottle brushes and is adjacent to the *Melaleuca* wetlands and natural *Eucalyptus* woodland. The *M. quinquenervia* flowers from late summer through autumn, and more *Eucalyptus* species flower in autumn, winter, and spring, than summer (Figure 2).

Sampling site

Equipment was sited at Rothwell in a typical suburban backyard of a privately owned home on a 1000 m^2 block of land. The air sampling pump was inside a covered shed with a Tygon tube extending outside, open to the air, and under the roofline, at adult head height. A pool was within 5 m, with foliage plants and lawn, not flowering during the sampling. Adjacent houses were similar. Typical verge plantings were *Callistemon viminalis*, "bottlebrushes". Figure 3 shows this Myrtaceae species that is commonly planted in public spaces and private gardens.

Figure 2 *Eucalyptus* flowers.

Sampling periods

Samples from 1 October until 15 December 2000 (spring) and from 1 April until 30 May 2001 (autumn) were collected three times per week. This new separate-season analysis was prompted by the 2016 thunderstorm asthma event that was discussed in the Introduction. Previous analysis of the combined season dataset was inconclusive and not offered for publication.

Figure 3 *Callistemon viminalis* (bottlebrush) in a railway carpark.

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Participants

Participants with doctor-diagnosed seasonal asthma, during the previous 12 months, were recruited via schools and newspapers. Participants numbered 20, 8 males and 12 females with and age range of 12–59 years: mean, 28 years; mode,14 years; and median, 18 years. Unpaid, they were of mixed ages and gender, all who volunteered were accepted. Spirometry was included in their assessment by a respiratory specialist, along with an ISAAC Questionnaire.

Regular medication usage was variable: some used both a preventer and a reliever, some a reliever only, and some neither. No adjustments were made for this variation, but preventer and reliever usage are two of the 12 dependent variables measured.

Participants reported using either salbutamol or salmeterol as their reliever medication (salbutamol was prescribed more frequently); fluticasone propionate or budesonide was prescribed with similar frequency for participants using preventer medication.

Non-smoking participants lived and worked in premises without air-conditioning, within a 20 km radius of Rothwell.

Respiratory diary measures

Self-report respiratory measures were recorded on a form sent monthly. After training, peak expiratory flow (PEF) was measured on new peak-flow meters, supplied. Upon waking, the best of three blows was recorded as the PEF, along with the ratings of the previous day's symptoms.

The "asthma score" was a 10-point ranked item:

> How is your asthma today?
>
> Write a number between 1 and 10 with '1' meaning 'very good' and '10' meaning 'terrible'.

The remaining nine items were 4-point ranks starting from '0' and extending to '3'. Participants were asked separately:

> Since your last peak flow have you been: coughing/wheezing/sneezing?
>
> Since your last peak flow have you had: difficulty breathing/an itchy nose/had itchy eyes/a runny nose/a blocked (congested) nose?

They were required to write "0," "1", "2", or "3" corresponding to "none", "a little", "a lot", and "most of the time" on the relevant date, marked in a table format.

Reliever and preventer usage were reported separately on three-point items:

> Have you increased or decreased your asthma reliever/preventer medication?
>
> Put 'I' for 'increased'; 'D' for 'decreased' and 'S' for 'stayed the same'.

When not using medication, they recorded "S", recommencing, they recorded "I" and ceasing they recorded "D". These were converted to −1, 0, and 1 for statistical analysis.

Dependent variables

Standardized (z) peak expiratory flow (SPEF), and symptom score group means were the dependent variables. Measures were: SPEF, asthma score, wheeze, cough, difficulty breathing (dyspnea), reliever usage, preventer usage, itchy eyes, itchy nose, runny nose (rhinorrhea), sneezing, and blocked nose (congested nose).

Independent variables

Air spora, compounds from air samples, pollutants, and meteorological variables served as independent variables. They were day length, mean atmospheric pressure, mean temperature, precipitation, mean wind speed, relative humidity at 9 am, particulates <10 microns (PM_{10}), heard thunder, ozone (O_3), nitrogen monoxide (NO), nitrogen dioxide (NO_2), Myrtaceae pollen, Poaceae pollen, *Pinus* pollen, Asteraceae pollen, *Casuarina* pollen, *Acacia* pollen, "other" pollen, *Cladosporium, Alternaria*, "other" fungi, benzoic acid, benzaldehyde, alpha pinene, beta pinene, 1,8 cineole, camphor, limonene, linalyl acetate, and linalool.

Floral and air and thunderstorm sampling

Independent variables of benzoic acid, benzaldehyde, alpha pinene, beta pinene, 1,8 cineole, camphor, limonene, linalyl acetate, and linalool were determined as ambient gases through floral and air analysis. Details of flower and air sampling and gas chromatography–mass spectrometry (GCMS) method and analysis, including chromatograms of the thunderstorm sample, and a typical air sample, are detailed in the supplementary information.

Statistical procedures

Statistical analyses were performed with SPSS Version 22. Procedures used were one-way ANOVA, principal components analysis, and general linear regression (GLM). Alpha was set at 0.05. Data was tested for homogeneity and normality and transformed where necessary. Univariate GLM analyses of group mean symptom scores and environmental measures on the same day, and up to 5 days of lag, predicted respiratory

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symptom responses. Univariate models maximize statistical power in a context of limited air sample data points. Relationships between heard thunder and volatile emissions were also investigated.

Transformations of air sample data

Air sample measures were transformed from the original categorically quantitative ratings assigned during analysis. The range from "nil" through to "very, very high" represents 10 categories which were converted to a 10-point scale, that was log10 transformed to approximate the quantitative increases of compounds in ambient air.

Results

Floral emissions before and after a storm

The supplementary information shows emissions from *Grevillea* "Robyn Gordon" captured before and after a storm. Included GCMS chromatograms demonstrate substantially increased linalool, hexenal, and hexanoic acid emissions before the storm, compared to after the storm, and relative quantities are listed.

Asthma and allergic rhinitis symptom summaries

Completion rate was 74% for completion of SPEF readings and symptom scores. Participants were asked to omit forgotten entries, rather than guess. Returns for spring were 20 October, 17 November, 11 December; average, 16. For autumn, 14 April, 14 May; average, 14.

For clarity, "at a glance" results charts, using symbols, have been created. Meaningful statistically significant ($p \leq 0.05$), relationships between individual symptoms and predictor variables from univariate linear regression models have been displayed in two charts, asthma symptoms, autumn and spring (Figure 4); and allergic rhinitis symptoms, autumn and spring (Figure 5). The external file 'Regression models.xlsx' contains univariate model information, including variance, for statistically significant relationships ($p \leq 0.05$) between individual predictors and 12 symptom measures, in spring and autumn, separately (Table S1).

Asthma symptoms

In autumn (Figure 4), decreased SPEF is predicted, at various lags, by decreasing day length, temperature ($0.0001 \leq p \leq 0.001$), and atmospheric pressure ($0.001 \leq p \leq 0.01$); increasing nitrogen monoxide ($0.0001 \leq p \leq 0.001$), *Acacia* (wattle) pollen and "other" fungi ($0.001 \leq p \leq 0.01$), alpha and beta pinene (lags 3,5), and 1,8 cineole (lag 3) ($p \leq 0.05$).

In spring (Figure 4), decreased SPEF is predicted by decreasing atmospheric pressure ($0.0001 \leq p \leq 0.05$); increasing day length and temperature ($0.001 \leq p \leq 0.05$), *Cladosporium, Alternaria*, and benzaldehyde ($p \leq 0.05$).

These results support BVOC emissions as mediating variables in explaining the relationships of decreasing atmospheric pressure, thunder, and increased symptoms. Heard thunder predicts different same day emissions in autumn (alpha and beta pinene adjusted R^2=0.18, p=0.03, df 1/21, F=5.8) compared to spring (linalyl acetate adjusted R^2=0.14, p=0.04, df 1/21, F=4.6).

Terpene emissions before thunder, before rain (precipitation), and in fine weather, are shown in Figure 6. Lower air pressure is associated with rain and storms, and higher pressure with clear skies and sunny conditions.[42] Relationships between atmospheric pressure and terpene emission are statistically neutralized by occurrence in both fine and stormy weather; so, thunder can predict BVOC emissions, but emissions cannot predict thunder, as they occur in fine weather too.

In autumn, increases in other asthma symptoms (Figure 4) are predicted, at various lags, by decreased day length, temperature, and atmospheric pressure ($0.0001 \leq p \leq 0.05$); increased NO_x, PM^{10}, pollens (Myrtaceae, *Acacia* and "other") ($0.0001 \leq p \leq 0.05$); "other" fungi and decreased humidity feature in fewer symptoms ($0.0001 \leq p \leq 0.01$). Increased camphor, linalyl acetate, and especially linalool, feature ($0.01 \leq p \leq 0.05$), as do the aromatic compounds benzaldehyde and benzoic acid ($0.001 \leq p \leq 0.05$).

For spring, increases in other asthma symptoms (Figure 4) are strongly and consistently predicted, at various lags, by decreasing atmospheric pressure and increasing temperature and day length ($0.0001 \leq p \leq 0.05$); and, increased Poaceae pollen predicts increased wheeze, difficulty breathing, and increased preventer use ($0.001 \leq p \leq 0.05$). Increased alpha and beta pinene, camphor, linalyl acetate, and linalool predict increased asthma score, wheeze, dry cough, and reliever usage; increased benzaldehyde predicts dry cough ($0.001 \leq p \leq 0.05$).

Asthma symptom predictors, common to autumn and spring

Decreasing atmospheric pressure is the only predictor ($p \leq 0.05$) of decreased SPEF for both autumn and spring.

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Figure 4 Asthma symptoms, autumn and spring.

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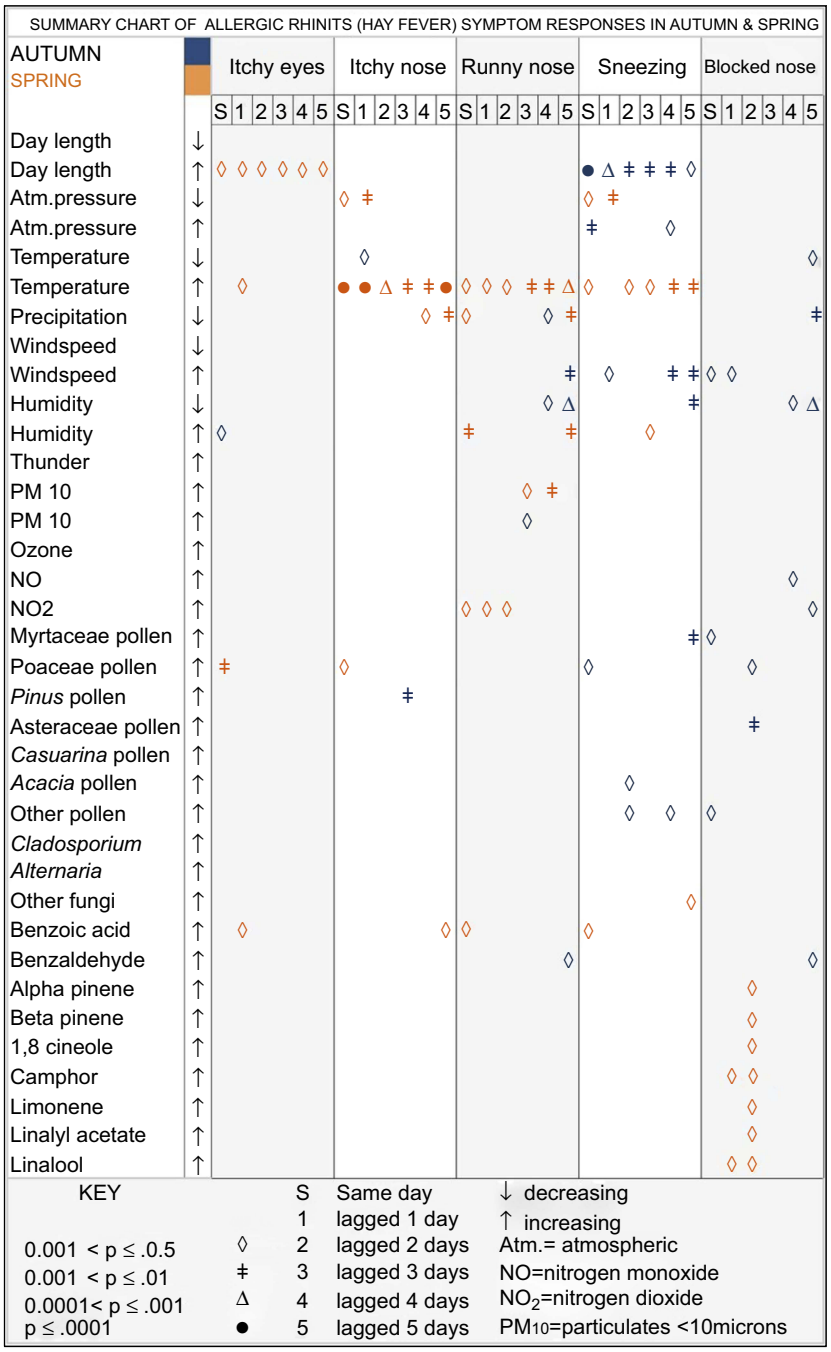

Figure 5 Allergic rhinitis symptoms, autumn and spring.

Asthma symptom predictors, common to autumn and spring (Figure 4), excluding SPEF, are decreasing atmospheric pressure, increasing NO_2, benzaldehyde, camphor, and linalyl acetate (variously, $0.001 \leq p \leq 0.05$). Note that some of the strongest effects for BVOCs, and asthma symptoms occur at lag 2 days and lag 5 days, suggesting an important delayed response (Figure 4).

Allergic rhinitis symptoms

Autumn allergic rhinitis symptom measures (Figure 5) show that increased day length and Myrtaceae pollen predicts sneezing ($0.0001 \leq p \leq 0.05$). Increasing wind speed and various pollens predict sneezing and "blocked" (congested) nose symptoms ($0.0001 \leq p \leq 0.05$). Increased atmospheric pressure, as occurs on a fine day, is predictive only of sneezing ($0.001 \leq p \leq 0.05$). Decreased humidity predicts

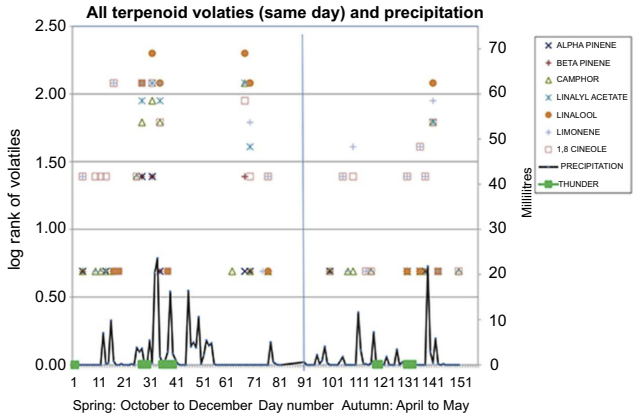

Figure 6 Terpene emissions before thunder, before rain, and in fine weather.

sneezing, runny nose, and "blocked" nose ($0.001 \leq p \leq 0.05$); increased humidity predicts itchy eyes only ($p \leq 0.05$).

In spring (Figure 5), increased temperature predicts AR symptoms and itchy and runny nose ($0.0001 \leq p \leq 0.05$). Increased Poaceae pollen, increased NO_2, and reduced precipitation, predict increases in AR symptoms ($0.001 \leq p \leq 0.05$). Increased day length only predicts itchy eyes ($p \leq 0.05$), and increased humidity predicts sneezing and runny nose ($0.001 \leq p \leq 0.05$). Increased "other fungi" predicts sneezing ($p \leq 0.05$). Increased benzoic acid is predictive of itchy eyes, itchy nose, runny nose, and sneezing in spring ($p \leq 0.05$). Congested ("blocked") nose in spring was predicted by seven terpenes after a two-day lag: alpha and beta pinene, 1,8 cineole, camphor, limonene, linalyl acetate, and linalool ($p \leq 0.05$).

Examining sampling bias

Are sample days different from days not sampled?

To investigate possible sampling bias, sets of alternate sample days were compared for SPEF readings to ensure that air sampling days, that occurred three times per week, were not different from days unsampled; one-way ANOVA was used. All possible days were divided into three sets: Set A (day 1, day 4, day 7, etc.); Set B (day 2, day 5, day 8); Set C (day 3, day 6, day 9, etc.). There was homogeneity of variances, as assessed by a one-way ANOVA (SPSS 22) (p=0.11), so sampling days were similar to days unsampled.

What is the daily sampling variance compared to every-third-day variance?

Table 1 compares Lag-3-day variances (because they predict SPEF reduction), comparing how each independent variable affects SPEF in a daily measure condition, compared to every-third-day measures. Variance for "temperature", "day length", "precipitation", and *Cladosporium* increases in the "air sample days" condition compared to "all days"; it remains unchanged for "Poaceae"; and, "other pollen", "*Alternaria*", "ozone", and "wind speed" are reduced.

Discussion

Increases of BVOCs from Australian trees predict respiratory symptom increases here. Figure 7 shows BVOCs plotted against same-day SPEF. Increases in the bicyclic monoterpenes, alpha and beta pinene, and the ketone, camphor, predict asthma symptoms, as does the acyclic alcohol, linalool, and its related ester, linalyl acetate. These compounds are similarly found in emissions from OSR crops (canola) ,[31] and conifers,[43] and many other plants, and are additional to predictors investigated by others previously.[14,18–20,44] Nasal congestion reported in response to seven terpenes in spring may be related to rhinosinusitis.[45]

Increases in the aromatic compounds, benzaldehyde and benzoic acid (Figure 8) also predict a range of symptoms here. Benzaldehyde is a sweet aldehyde that attracts pollinators and is a sensitizer;[40] benzoic acid has been associated with various contact sensitivities.[46] Safety for these has not been established where inhalation is an exposure route.[47,48] These compounds are used widely in food and cosmetics;[48] many are commonly found in sensitizing fragrance and personal hygiene products.[49]

Floral emissions consist of complex blends, but little is known about synergistic effects; however, Juergens reports that any positive effects of 1,8 cineole for respiratory health[50,51] would likely be countered by the presence of pinene, trapped here, to which Juergens attributes adverse reactions to *Eucalyptus* oil.[52]

Respiratory response to pinenes has been studied for decades,[53–55] often in the context of lumber mill workers. Camphor and pinene may also have a role as apoptosis blockers. Eosinophilic inflammation of the airways is a key characteristic of asthma and eosinophils accumulate in part because of their prolonged survival.[56] Apoptosis, or programmed cell death, is important in the removal of eosinophils from the lungs.[57] Impaired apoptosis has also been implicated in increased rhinovirus replication,[58] thus contributing to prolonged periods of illness for people with asthma. Terpene emissions may influence apoptosis.

This study showed that pinene and camphor predict reduced SPEF (Figure 9) and increased medication usage, respectively. It is known that (+)-alpha-pinene is structurally related to (+)-camphor.[32] Pro-apoptotic applications of terpenes abound in the literature, but there are some apoptosis

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Table 1 Variance comparison of daily versus three-per-week air samples

Predicting SPEF in autumn comparing "three days per week" and "every day" sampling										
	Lag 3 Air sample only (3 days)					Lag 3 every day				
	RSq	Pr>F	df	F	Dir	RSq	Pr>F	df	F	Dir
Daylength	0.35	0.00	1.20	10.6	POS	0.21	0.00	1,56	14.9	POS
Mean atm pressure	0.16	0.06	1.20	3.9	POS	0.12	0.01	1,56	7.5	POS
Mean temperature	0.24	0.02	1.20	6.3	POS	0.11	0.01	1,56	6.7	POS
Precipitation	0.16	0.07	1.20	3.8	POS	0.01	0.37	1,56	0.8	NEG
Mean windspeed	0.00	0.99	1.20	0.0	POS	0.03	0.17	1,56	1.9	POS
PM10	0.03	0.45	1.20	0.6	NEG	0.01	0.52	1,56	0.4	NEG
Ozone	0.00	0.96	1.18	0.0	POS	0.04	0.14	1,56	2.3	POS
NOX	0.04	0.36	1.20	0.9	NEG	0.02	0.25	1,56	1.4	NEG
NO2	0.04	0.35	1.20	0.9	NEG	0.01	0.42	1,56	0.7	NEG
Relative humidity	0.13	0.10	1.20	3.0	POS	0.01	0.42	1,56	0.7	POS
Myrtaceae pollen	0.12	0.12	1.20	2.7	POS	0.05	0.11	1,52	2.6	POS
Poaceae pollen	0.06	0.27	1.20	1.3	POS	0.06	0.08	1,52	3.3	POS
***Pinus* pollen**	0.04	0.35	1.20	0.9	NEG	0.01	0.50	1,52	0.5	NEG
Asteraceae pollen	0.01	0.60	1.20	0.6	POS	0.04	0.13	1,52	2.3	POS
***Casuarina* pollen**	0.05	0.30	1.20	1.1	NEG	0.01	0.49	1,52	0.5	NEG
***Acacia* pollen**	0.02	0.57	1.20	0.3	POS	0.01	0.50	1,52	0.5	POS
Other pollen	0.13	0.10	1.20	3.0	POS	0.14	0.01	1,52	8.4	POS
Cladosporium	0.05	0.34	1,20	1.0	POS	0.01	0.45	1,52	0.6	POS
Alternaria	0.01	0.66	1,20	0.2	POS	0.03	0.23	1,52	1.5	POS
Other fungi	0.00	0.93	1,20	0.0	POS	0.00	0.86	1,52	0.0	NEG
Benzoic acid	0.01	0.73	1,20	0.1	NEG					
Benzaldehyde	0.08	0.20	1,20	1.7	NEG					
Alpha pinene	0.22	0.03	1,20	5.5	NEG					
Beta pinene	0.22	0.03	1,20	5.5	NEG					
1, 8 cineole	0.20	0.04	1,20	5.0	NEG					
Camphor	0.09	0.19	1,20	1.9	NEG					
Limonene	0.16	0.06	1,20	3.9	NEG					
Linalyl acetate	0.03	0.44	1,20	0.6	NEG					
Linalool	0.14	0.09	1,20	3.2	NEG					

Abbreviations: SPEF, Standardized Peak Expiratory Flow; Lag 3, lagged three days; R Sq, R squared (variance); Pr, probability; df, degrees of freedom; F, F statistic; Dir, direction; Pos, positive; Neg, negative; PM_{10}, particulates less than 10 microns; NO_x, nitrogen monoxide; NO_2, nitrogen dioxide.

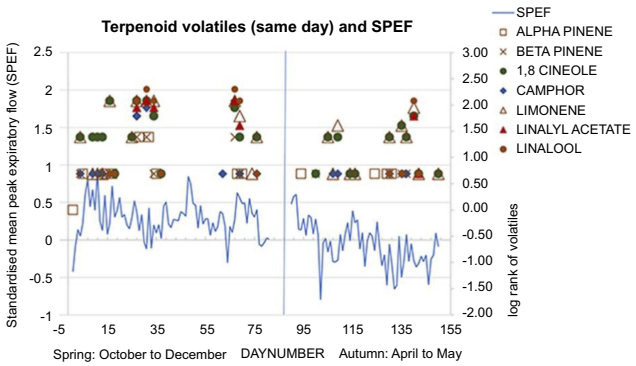

Figure 7 Terpene BVOCs (same-day) and SPEF.
Abbreviation: BVOCs, biogenic volatile organic compounds.

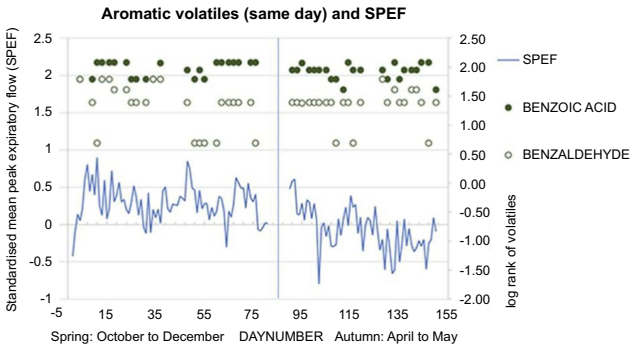

Figure 8 Aromatic volatiles (same-day) and SPEF.

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blockers—they involve these same terpenes. Nakano found that camphor inhibited apoptosis in human oral tumor cells when other ketones induced it.[59] Na et al[60] examined the effect of juniper oil on apoptosis in human brain astrocytes. Heat shock–induced apoptosis of these cells was blocked by pretreatment with juniper oil. Juniper oil typically consists largely of pinene.[61]

Increased VOC emission may be influential in "thunderstorm asthma". Sweet floral compounds have long been associated with allergic responses.[62,63] Heard thunder predicted the release of some terpenes in autumn and spring. This could be due to the reduction in atmospheric pressure, as occurs with storms, resulting in the effusion of volatiles at that time, as with aquifers' levels and tidal flows.[64,65] Thunder is associated with storms in which air pressure plummets. For plants, stages of growth are influential as in cattle gorging on toxic larkspur flowers before a storm.[30] Sweet honey–fragranced linalool is a ubiquitous terpene emitted from flowers and was captured in a markedly increased amount in this study from a *Grevillea* during a storm event; spring thunder predicts the occurrence of the related sweet ester, linalyl acetate, in air samples. Hexenal, a aldehyde sensitizer, is emitted when grass is cut,[66] and also by the *Grevillea* flower sampled here before the storm. Asthma and lawn mowing has been associated for decades,[67] but the association of BVOCs with both is new.

Heard thunder did not predict respiratory symptoms. Why? From days 55 to 75, there is no rain and yet SPEF drops markedly, and emissions are substantial (Figure 6). Fine weather neutralizes any statistical relationship for thunder and respiratory response, so "thunder heard" did not predict any symptoms. This work reveals a strong relationship between increasing severity of respiratory symptoms and atmospheric (barometric) pressure. The great majority of significant relationships ($p \leq 0.05$), 43 of them, involve reducing pressure and only two increasing pressure. Thus, increased respiratory symptoms, and increased BVOCs, can occur on both fine days, with no rain, and on rainy and/or stormy days.

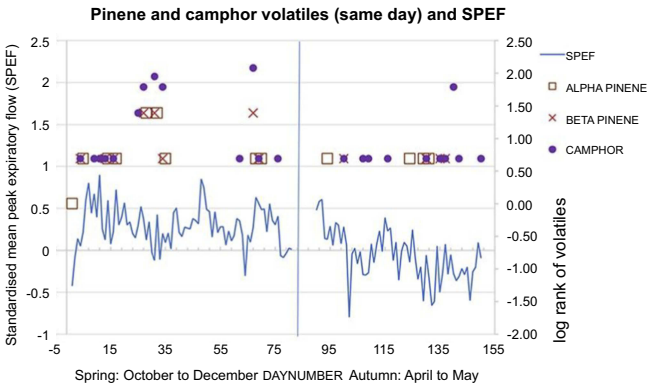

Figure 9 Pinene and camphor volatiles (same-day) and SPEF.

Asthma occurs in environments with varied temperatures but the highest prevalence is in the temperate zones of world.[68] Others[44,69] report asthma increasing both in cooler and in warmer conditions too. This paradox can be explained by optimal flowering of plants that may be related to respiratory response. Floral terpene emission is related to light and temperature,[70] interactively,[71] though the influence may only be an indirect one: developmental staging (ontogeny)—new growth, flowering, senescence—strongly governs emissions.[31,72,73] Maximum floral terpene emissions occur at the optimal temperature for flowering.[74] For winter flowers that temperature will be lower than for spring or summer flowers. Emissions will occur at increasing and decreasing temperatures because of species' flowering needs.

Increasing and decreasing temperature significantly ($p \leq 0.05$) predicts respiratory symptoms in this study. *M. quinquenervia* flowering occurs at decreasing temperature and increasing respiratory symptoms in autumn; *Eucalyptus, Melaleuca leucadendra, and Callistemon viminalis* flowering occurs at increasing temperature and respiratory symptoms, in spring, along with other Myrtaceae and many other plants.

Limitations

Subsequent studies will benefit from increased participants. Increasing air sampling from three to seven days per week would enhance analysis by providing more data points, thereby increasing statistical power and enabling multivariate analysis. This is related to funding, access, equipment security, and distance issues.

Terpenes occur in vast numbers and combinations; identifying them in ambient air is a complex procedure. Here, volatiles from ambient air were reported using quantitative approximations and only the most frequently occurring were used in analyses. It is possible that the most influential were not identified because they were not frequently occurring, nor in larger quantities. This can be rectified by increased funding and increased analysis of BVOCs. Employing chemical standards daily would enhance precision in quantification of the volatiles measured. This specialized addition would require a considerable input of expertise and funding. Laboratories equipped for this are rare, requiring well-stocked chemical libraries.

Using 10-point scales in all the self-report symptom and medication usage scales would increase the sensitivity of the statistical analysis. To extend to a year-long project, with

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seasonal analysis, would enhance understanding of volatile patterns and respiratory relationships. The growing body of work regarding SOA's that result from oxidation of volatiles trapped in this project shows that this issue is complex and may take some time to clarify and evolve.

Conclusions

Here, a range of respiratory symptoms are predicted by BVOCs trapped in ambient air. Univariate regression models demonstrate strong relationships with natural drivers of floral processes and BVOC production: day length and temperature.

When anthropogenic pollutants combine with BVOCs, the potential for the generation of toxic compounds is increased. Nitrogen oxides confound the SPEF analysis results in autumn, when pinene is featured, due to the annual seasonal increase of NOx in cooler months. Determining relative contributions of these components is beyond the scope here due to the limitation in the number of air samples and statistical convention. The formation of secondary organic aerosols from combinations of NOx and pinenes,[75] trapped here, highlights the importance of this co-occurrence.

Researchers have noted allergic responses with domestic usage of the fragrance products like lavender oil,[34] which contains linalool and linalyl acetate; emission of these was predicted by heard thunder in this study. These emissions were predictive of increased asthma symptoms and medication usage in both autumn and spring here. Tea tree oil (from *Melaleuca alternifolia*) autoxidizes to form allergens too[76] and is widely used domestically. *Eucalyptus* oil is not safe for those with respiratory sensitivities and pinene, detected here, is the attributed reason,[52]due to its tendency to form harmful peroxides and increased pro-inflammatory mediators.

Continuous monitoring of plant emissions can be achieved[77] to reveal seasonal patterns and enable protection for the vulnerable. BVOCs vary with the vegetation, and its developmental stage: emissions from a desert[78] will differ from a *Eucalyptus* forest,[77] or a rose garden.[79] Results here are specific to this locality and will differ from another. Future research needs to accommodate these variations of geography, season and weather.

Anecdotally, Australian plants, and others are associated with respiratory symptoms; this work supports that. Informed practice and botanical diversification are needed, especially in and around child care centers, schools, and aged care facilities that are occupied by those most vulnerable to respiratory stressors. Public landscaping could better utilize foliage plants and/or informed floral choices. For health professionals, there is much to do in educating the community about potential negative effects of using essential oil products, for those vulnerable to respiratory symptoms.

This work provides a basis to employ: asthma alerts based upon real-time measures of BVOCs;[77] diversity in domestic and urban landscaping, and gardening practices; discerning essential oil product usage; and thoughtful positioning of housing developments, when near some crops and forestry plantations. Most important, the effects of global warming, and temperature increases, as they impact plant emissions,[2] need to be included in future health models incorporating BVOCs.

This is a new page in the book of environmental asthma research and provides a basis for others to continue to investigate the effects of BVOCs. Already, pollen and pollution variables have been identified as contributing to asthma and allergic rhinitis; this work adds BVOCs to the list of environmental stressors that can reduce respiratory health. Further, it provides some rationale for the seasonality of effects and enhances understanding of the role of day length, temperature, and atmospheric pressure. The link between temperature and plant emissions invites further research to inform and minimize negative respiratory impact and maximize health, especially for the most vulnerable people in our communities.

Ethics approval and informed consent

Ethics approval was sought and obtained from the Griffith University Human Research Ethics Committee. All methods were performed in accordance with the relevant guidelines and regulations from Griffith University. Informed written consent was obtained from adults, and parents or guardians, and children/minors.

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Disclosure

The author reports no conflicts of interest in this work.

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