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Human symptom responses to bioeffluents, short-chain carbonyls/acids and long-chain carbonyls in a simulated aircraft cabin environment

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Abstract

Occupants of aircraft have reported an array of symptoms related to general discomfort and irritation. Volatile organic compounds (VOCs) have been suggested to contribute to the reported symptoms. VOCs are from products used, bioeffluents from people and ozone reaction products. Thirty-six healthy, young female subjects rated symptoms and environmental quality during an 8-hour exposure to groups of compounds often present in aircraft: 1) long chain carbonyls, 2) simulated bioeffluents, and 3) short chain carbonyls/organic acids. Statistically more symptoms were identified for the simulated bioeffluents and, to a lesser extent, short chain carbonyls/organic acids compared to a control condition, though they remained in the acceptable range. There were three temporal patterns in the environmental quality and symptom reports: 1) an adaptive response (immediate increases followed by a decline); 2) an apparent physiological effect (increases one to three hours into the exposure that remained elevated) or 3) no statistical differences in reported environmental quality or symptom severity compared to the control air conditions. Typical concentrations found in aircraft can cause transitory symptoms in healthy individuals questioning the adequacy of current standards. Effects on individuals sensitive to air pollutants and methods to remove the compounds causing the greatest symptom responses are needed.

Keywords

Aircraft cabin; bioeffluents; symptom reports; controlled study; VOCs

Background and Objectives

Exposures to mixtures of volatile organic compounds (VOCs) have been associated with complaints about air quality, increased reports of transient symptoms and adverse health

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effects in enclosed environments, particularly aircraft cabins.¹⁻⁴ VOCs that off-gas from materials have often been reported as one culprit for poor air quality;⁵ chemical reactions with ozone that enters from outdoors produce secondary pollutants that can be irritating;^{6, 7} and bioeffluent organic compounds emitted from people can result in perceived poor air quality and feelings of malaise.^{8,9} Bioeffluent compounds include carbonyls, alkyl alcohols, aromatic alcohols, ammonia, and mercaptans.^{3, 10} To provide good indoor and enclosed environment air quality, ventilation standards have been developed based on occupancy in office buildings. For commercial aircraft a minimum amount of outside air of 0.55 pounds per minute per person (0.28 cubic meters per minute of air at 2,400 meters pressure altitude and at cabin temperature of 24 °C) is required to augment the HEPA-filtered recirculated air in a commercial aircraft and for certain flight paths converters to remove ozone are installed. These ventilation standards are designed in part to reduce human bioeffluent air concentrations, particularly odiferous compounds^{11, 12} and other indoor pollutants. In airplanes, the ventilation rate results in a carbon dioxide (CO₂) level of approximately 1500 ppm, comparable to other high-density indoor environments such as auditoriums, conference rooms, class rooms, buses, commuter trains and subways. Carbon dioxide (CO₂), a measure of human metabolism, is often used as a surrogate for bioeffluent levels and has been used to indicate acceptable air quality and sufficient ventilation for indoor building settings.¹⁰ The Federal Aviation Administration (FAA) Federal Aviation Regulation specifies that it should not exceed 5000 ppm in aircraft cabins to protect for occupant health, (FAR 25.831 (b2)). This covers aircraft that carry dry ice in galley carts to cool food and beverages. This is a CO₂ specific requirement and not established to serve as a surrogate. However, other bioeffluents are likely responsible for complaints about odors, irritancy, stale air, and stuffiness³ and may lead to the symptoms reported on aircraft. Levels of carbon dioxide above 1000 ppm may also increase reports of headaches, tiredness and perceived poor air quality in healthy adults.¹³

The aircraft cabin is an enclosed environment that presents unique challenges for maintaining acceptable air quality and a comfortable environment.²⁻⁴ These include achieving appropriate thermal comfort and humidity levels, as well as dealing with high occupant densities and limited mobility for the passengers and crew members. Within the aircraft cabin thermal comfort at times does not meet the ASHRAE standard for thermal comfort in non-industrial buildings and the relative humidity (RH) is typically lower (<20%) than most indoor settings (ASHRAE Standard 62.1-2013). These environmental conditions have been suggested to cause dry eyes and the low comfort levels that can be experienced on aircraft.¹⁴⁻¹⁷ Surveys of crew members and passengers flying on planes have reported a variety of transient symptoms, such as ocular and respiratory irritation, headaches, fatigue and dizziness.^{6, 16} In particular, the low RH typical of the aircraft cabin environment has been implicated in causing many of the transient symptoms reported.^{8, 18} However, controlled exposure studies that mimic some of the air quality and environmental conditions on aircraft have suggested that VOCs present in the aircraft cabin also contribute to the reported symptoms.^{3, 7, 15, 19} Symptoms reported to be associated with poor air quality include respiratory and ocular irritation, general malaise, headaches, and poor concentration.

Numerous organic compounds have been identified or are expected to be present in the passenger cabins of commercial aircraft.²⁰⁻³⁰ These include compounds emitted directly

from products used on aircraft for cleaning, offgassing of materials within the aircraft, infiltration of chemicals from the outdoor air (e.g. kerosene fumes, deicing fluid, jet and diesel exhaust while on the ground), ozone at elevated altitudes, and bioeffluents from passengers. Ozone that penetrates into the aircraft cabin reacts with unsaturated hydrocarbons present on the skin of people and on surfaces producing by-products that can be irritating.^{7, 29, 31} In particular, ozone by-products include creating or modifying carbonyls in the air of indoor settings in addition to the aircraft cabin that can be irritating and cause headaches, general malaise and lower a person's ability to concentrate, which can be of concern to aircraft passengers.^{6, 20, 32–34} While we incorporated several of these carbonyls in our evaluation, many additional compounds can be produced from ozone reactions. If properly maintained ozone scrubbers are not used, ozone levels in the aircraft cabin can be high when the flight paths are at high elevations (>10,000 m) or for planes flying at lower altitudes if stratospheric air penetrates into the troposphere.

More than 8 million people fly on commercial aircraft each day with approximately 5% having preexisting respiratory disease.³⁵ Thus, it is necessary to provide high air quality in aircraft to protect public health. No study has examined which compounds or classes of compounds are potentially responsible for the symptom reports. The present study compares symptom and environmental quality ratings by subjects in a control condition which has filtered air at sea level, to those ratings reported during exposure to three different combinations of compounds normally present in aircraft cabins during flight and also often present in other indoor settings: 1) short chain carbonyls and organic acids, 2) long chain carbonyls and 3) simulated bioeffluents. These results can be used to provide guidance to ensure a healthy and comfortable environment within the aircraft cabin and other enclosed and indoor settings.

Methods

Controlled Environmental Facility

The exposures were conducted in the Controlled Environmental Facility (CEF) of the Environmental and Occupational Health Sciences Institute (EOHSI)/Rutgers University. The CEF is a 2.2 m high by 4.1 m wide by 2.7 m deep stainless steel room with a volume of 25 m³. It is equipped with a one-pass ventilation system into which VOCs are introduced at a controlled rate so that predetermined air concentrations of these VOCs can be maintained over extended time periods. The ambient air supply is filtered through both activated charcoal and a HEPA filter system to remove ambient air pollutants prior to the air entering the CEF. The air is not re-circulated and the maximum ventilation rate (700 cfm resulting in 48 air changes per hour) was used so that volatile compounds emitted from materials or people within the CEF were rapidly removed during the exposures. Thus, the exposures were dominated by the target chemicals introduced into the air and not likely to be from emissions by the subjects or furnishings within the CEF. The target chemicals, dissolved in either methanol or water, were injected into a heated (250 °C) glass round bottom flask at a constant flow rate using a Sage Instrument syringe pump (Model 355) rapidly vaporizing the target compounds and solvent. The vapors were flushed from the heated flask, using filtered compressed air, into a heated transfer line that is connected to a manifold above the inlet of

the CEF. The manifold contains baffles to mix the air before it enters the CEF through several dispersion units. A series of small fans are located on the ceiling of the CEF to facilitate the mixing of the air within the CEF. The total hydrocarbon air concentration was monitored continuously using a Teldyne total hydrocarbon analyzer (Model 420R) to verify in real time that the syringe was delivering the expected total organic compound concentration to the CEF. Adsorbent trap samples were collected at various times during the exposure to confirm the presence of the individual compounds at the target concentrations within the CEF. The temperature and RH of the CEF were maintained at 23 ± 2 °C and $15\pm 10\%$, respectively, conditions common within an aircraft cabin. Ozone was not measured in the CEF as these exposures were conducted between December 2008 and March 2009 and between December 2009 and January 2010 when ambient ozone levels in New Jersey are typically low (during the study, ozone levels on 3 days were <30 ppb, on 13 days 30–39 ppb and on 4 days 40–42 ppb). Ozone levels within the CEF have been found to be <50% of the ambient levels due to the charcoal filtering of the air. Ozone levels of <20 ppb are not expected to cause symptoms in healthy individuals and form only minimal amounts of long chain carbonyls at the high air exchange rates used during the experiments. Three rows of three airline seats each were placed in the CEF to simulate the seating conditions within airplanes (Figure 1). Nine subjects were accommodated at each of the four exposure sessions: control condition and three different chemical mixtures representative of long chain carbonyls, short chain carbonyls/organic acids, and simulated bioeffluents (Table 1). Each exposure session was eight hours from the time the subjects entered the CEF until they left. The chemical groups were introduced after the subjects had settled in their seats and completed an initial questionnaire. The sessions were separated by one week and the order of exposure sessions was different for the different groups of participants to minimize effects on symptom reports that might be associated with whether participants had previously spent time in the CEF.

Subject Recruitment

A total of 44 healthy, non-smoking women, aged 18–45 were recruited but results are reported from only 36 due to an equipment failure during one experiment with 8 subjects (Table 2). Healthy was defined as women without serious illnesses (for example: neurologic disease or brain injury, stroke or cardiovascular disease, serious pulmonary disease including asthma, liver or kidney disease, serious gastrointestinal disorder, known endocrine disease, and psychosis, bipolar disorder, alcoholism or drug abuse). Additionally, the subjects were neither pregnant nor lactating.

Women were selected as subjects primarily because previous studies have shown women tend to report more symptoms from exposure to poor air quality than men.^{36, 37} However, we did not check to determine if the subjects in this study consider themselves sensitive to exposure to air pollutants or odors.

Subjects were solicited through advertisements placed in a Rutgers University student newspaper and posting flyers outlining the study in common areas of campus buildings. Potential subjects who contacted our recruiting office were asked screening health questions after a verbal informed consent was given to ascertain that they met the health status

requirement and were available to attend four full day sessions. If a subject met the screening criteria for participation, she was invited to attend an initial session to complete a screening physical examination, be shown the CEF and provided details on the study procedures, including instructions on completion of the questionnaires. Subjects for whom exclusionary health conditions were identified during the physical examination were informed about these findings by our physician and excluded from participation. The study was approved by the University's Institutional Review Board.

Compound Selection

Three groups of compounds that are prevalent in an aircraft cabin, and could elicit reversible symptoms were evaluated along with a control condition (Table 1). The concentrations of the compounds were selected to be at the upper concentrations expected in aircraft cabins, and likely exceed their odor thresholds, but not cause irreversible adverse health symptoms. The compounds were grouped together based on similar chemical properties so that they could effectively be removed from the air together by a single filtration technique to improve air quality.

Chemical Analysis

Two types of air samples were collected: an adsorbent trap consisting of layered beds of charcoal and Tenax, which was thermally desorbed into a gas chromatography/mass spectrometry instrument, for the long chain carbonyls, simulated bioeffluents (except carbonyls) and sulfides; and a 2,4-dinitrophenylhydrazine (DNPH) cartridge, which was solvent extracted and analyzed by HPLC-UV, for short chain organic acids and carbonyls.

Symptom Questionnaire

A questionnaire previously used to characterize symptoms of subjects in simulated aircraft cabin air,^{7,29–31} was modified to include symptoms of anxiety, upper respiratory and lower respiratory function, and cognitive function. In addition, somatic control symptoms not expected to be associated with poor indoor air quality were also included. The symptom questionnaire was administered to ascertain the participants' ratings of environmental quality and health symptoms periodically throughout each exposure session (Supplemental Information). Subjects were given written instructions on how to mark their ratings and encouraged to mark their responses across the entire scale according to what she was feeling each time the questionnaire was being completed (example of scales used given in supplementary data). The environmental quality and health symptom ratings used a visual-analogue scale with labels at each end of the scale (i.e., end labels) and a break in the middle forcing a decision between "acceptable" and "unacceptable" (see Figure 1 of Strøm-Tejsen et al.⁷). Responses were scored by physically measuring the subject's mark to within 1 mm. Air quality, thermal environment, air movement, and noise level were rated from clearly unacceptable to clearly acceptable. Odor intensity, eye irritation, nose irritation, and throat irritation were rated from no symptom to overpowering. Thermal environment was rated using a 7-point scale ranging from cold to hot. Humidity, air freshness, lighting, and noise were rated from too dry, air fresh, too bright, and too noisy, respectively, to being acceptable. Higher scores at the scales' end labels were indicative of greater symptoms.

Subject Protocols

On the day of the first session, the subjects reported to the EOHSI clinic and were checked by a nurse to confirm that they were healthy on the day of testing (i.e., no upper respiratory illness, flu, or active allergy). The subjects were not restricted in the use of any personal care hygienic products, e.g. deodorants, shampoos, perfumes, on the day of an exposure session. A preliminary questionnaire was administered in the clinic before the participants entered the CEF. Questionnaires were then administered after the participants took their seats in the CEF but before the exposure started (baseline), and at 10 minutes and one, three, five, and seven hours after exposure onset, and finally in the clinic after leaving the CEF. The technician monitoring the exposure session prompted the subjects to complete the questionnaire by making an announcement over the intercom reiterating the instructions for questionnaire completion. Prior to leaving for the day, the subjects completed a debriefing questionnaire and a medical clearance questionnaire as part of the safety protocols for participating in the study. The participants were provided with snacks, sandwiches and drinks, similar to those provided on “economy” flights of eight hours in duration. The food selection was from a local caterer to standardize the types of food eaten. A restroom is attached to the CEF. While in the CEF, participants were visually monitored through a one-way mirror by the researchers to assure their safety. The participants were allowed to use computers, listen to music, watch movies and read books, in a manner similar to what would occur in an aircraft.

Study Design and Statistical Analysis

A within subjects repeated measures design was used to ascertain whether any of the three chemical mixtures -- simulated bioeffluents, short chain carbonyls/organic acids and long chain carbonyls -- elicited a symptomatic response that differed from the control condition. The analyses for this paper were performed using the SAS/STAT software, Version 9.4 of the SAS System for Windows. Means and standard deviations were calculated for the severity of each symptom at all of the time points when the questionnaire was administered. In addition, means of the changes from baseline were calculated. Scores were checked for normality and log-transformed. Mixed linear models, with random intercepts for individual, examined effects of exposure on responses at each time point as well as changes from baseline to each time point, with post-hoc pairwise comparison of each exposure to the control condition. Significance was defined as $p < 0.05$. We note that no multiple testing corrections have been applied. However, multiple testing problems should be considered in interpreting these results. Non-parametric, Wilcoxon matched-pairs signed rank tests were also conducted to allow direct comparison with the statistical analyses reported in previous studies⁷. In particular, a Wilcoxon signed-rank test evaluated whether the median differences between the exposure and control conditions in either the symptom at each time point or the change from baseline differed from zero. These results are provided in the Supplementary Information. We note that in some cases, the nonparametric tests revealed significant findings where the ANOVA findings were non-significant. In the majority of these cases, fairly large outliers led to inflation of the estimated standard errors. Because we had three exposures and a control condition, the ANOVA was employed in order to take full advantage of the information from all scenarios to get more stable estimates of the error and to allow for separation of random error versus error due to an individual subject in

estimation of the error terms. Note that the difference in scores between the baseline and each time point for each exposure session controlled for intra-day differences that a subject might report based on how she was feeling at the start of the day. This intra-day difference could affect the absolute score at each time point. The syringe pumped leaked during one session of long chain carbonyl exposure resulting in lower than expected exposures during part of that session. The data from that group of subjects were therefore excluded from the analyses resulting in a final n of 36 subjects.

Results

Chemical Exposures

The exposures were monitored using a real time total hydrocarbon analyzer (THC) and observation of the syringe flow rate. The THC trace showed the expected spikes in total hydrocarbon responses when subjects first entered the CEF or opened food packages during the meals. These increases in total hydrocarbon levels were transitory. The mean measured air concentrations are given in Table 3. The proper syringe flow rate setting and corresponding air concentrations were verified prior to the initiation of the controlled exposures. The concentration of at least one compound was confirmed in each group which was delivered as a single mixture prepared from neat stock solutions. Several of the simulated bioeffluent compounds (dimethyl sulfide, ethyl mercaptan and propyl mercaptan) had target concentrations ($<5 \mu\text{g}/\text{m}^3$) below the detection limit for the air volume sampled. However, each session did have several compounds whose concentrations were confirmed to be in the target range, and all target compounds were present at predetermined ratios in a single liquid mixture, and hence were delivered at these known ratios.

Environmental Qualities and Health Symptoms

The responses to the baseline questionnaire administered when the participants entered the CEF prior to the introduction of any of the chemical groups were not significantly different across the four conditions (Table 4). This indicates that on average the participants did not have differential symptom responses or environmental quality ratings at baseline for any given exposure condition.

Without adjusting for baseline, exposure to simulated bioeffluents resulted in the greatest number of symptoms and ratings of environmental quality that were significantly different from responses reported for the control exposure session (Table 4). After adjusting for the baseline responses, the results were essentially unchanged with the exception of noise which was statistically different only in the unadjusted score evaluation and eye irritation and throat irritation which were statistically different only in the baseline adjusted analyses. The symptom scores reported in the questionnaire administered in the clinic after the end of the bio-effluent sessions were not statistically different from the baseline symptom scores, indicating that symptoms returned to baseline within minutes of the exposure ending. Symptoms with statistically significant differences from the control condition were all in the direction of being less acceptable (e.g. poorer air quality, more irritation) for the simulated bioeffluent sessions at multiple time points after the introduction of the chemical, though the symptoms reported were still considered to be within an acceptable range by the subjects.

Thus, while the introduction of the simulated bioeffluents increased the symptom reports, the magnitude of the effect did not require any medical attention nor was it sufficiently problematic for any of the healthy subjects to request ending her participation in the study.

Exposure to short chain carbonyls/organic acids resulted in increased symptom scores for eye irritation, nose irritation, eyes dry, and headache and reduced perceptions of environmental quality for air quality, odor intensity and air freshness compared to the control session at multiple time points for both the unadjusted and adjusted comparisons. Symptom scores reported in the questionnaire administered in the clinic after the participants were removed from the exposure to the short chain carbonyls/organic acids returned to the baseline scores for all symptoms except for eye irritation which was still statistically higher. The symptom scores and environmental quality ratings during and after exposure to long chain carbonyls were not consistently statistically different from those reported during the control session for either the baseline unadjusted or adjusted analyses. Differences at individual time points could be random effects due to multiple comparisons rather than true changes in symptom scores.

Discussion

Responses to Exposures

At the exposure concentrations used, exposures to simulated bioeffluents and short chain carbonyls/organic acid mixtures, caused a significant increase in symptoms related to mucous membrane irritation and dryness (eye, throat), and headache, while exposure to long chain carbonyls had little to no effect on ratings of symptoms. Similarly, exposure to simulated bioeffluents and short chain carbonyls/organic acid mixtures resulted in reduced ratings of air quality that did not occur for the long chain carbonyl exposure condition. Predictions of irritation and symptom responses by compounds have been modeled based on their physical chemical properties that govern their partitioning into mucus membranes of the eye, nose, throat and lung, absorption into the body and reaction with the receptor that elicits the irritation responses.^{41–44} The key physiochemical properties considered include molar refractivity (a measure of total polarizability), dipolarity, hydrogen bond acidity and basicity, solubility in a lipid solvent, and proximate size of the molecule. The irritation response is dependent on the acidity or alkalinity of the agents, reactivity to proteins, oxidizing potential⁴⁵ and reactivity at receptor sites for toxicological effects.⁴⁶ The short chain carbonyls/acids have greater solubility in the mucus membranes and are more acidic than the long chain carbonyls. This would result in a higher percentage of their vapors dissolving in the mucous membranes of the eyes and respiratory tract. Their greater dissolution, higher overall target/aircraft cabin concentrations, coupled with most of them having lower odor thresholds than the long chain carbonyls, is a likely explanation for the greater symptom response reported by the subjects. In addition, several of the short chain species – formaldehyde, acetaldehyde, acrolein and formic acid – have been reported to be more irritating than the long chain species, though at high enough concentrations the latter can be ocular and respiratory irritants.⁴⁷

The irritant properties of the sulfur-containing compounds used to represent bioeffluents have not been included in the models comparing irritation of volatile organic compounds as

those studies have focused more on chemicals used in industrial settings or released into or formed photochemically in the ambient air. The sulfur compounds used are polar molecules that are acidic so would be expected to partition into the mucus membranes of the body. They have the lowest odor thresholds of the compounds studied and are reported to be ocular, respiratory and dermal irritants and to cause headaches at ppb levels.^{48–51} Phenol, also known as carbolic acid, is the other component of the simulated bioeffluent mixture. In addition to being acidic, it is a respiratory and ocular irritant and is quite soluble in mucus membranes.⁵² Simulated bioeffluents have been reported to cause the types of symptoms evaluated in this study⁹ and have been the rationale for setting minimal air exchange regulation and guidelines for occupational and residential settings and aircraft cabins. However, the FAA ventilation standard (FAR 25.831(a)) which is designed to prevent exposure to harmful concentrations of gases or contaminants, provide reasonable passenger comfort and minimize undue discomfort and fatigue of flight attendants also includes a limit for CO₂ (FAR 25.831(b2)). The aircraft cabin provides a setting where individuals are predominantly resting so their CO₂ emissions will be from basal metabolism, there is little distance between people, and the density of people per volume of air is greater than most enclosed or indoor setting commonly encountered but similar in density to buses, commuter trains, subways, auditoriums and conference rooms. However, the airflow per surface area is substantially higher in aircraft compared to most other environments, resulting in lower air contaminant levels originating from emissions from surfaces in aircraft.

Temporal Trends in Symptom Reports

The manner in which the symptoms changed with time within a session was examined visually. Three patterns are evident: i) an immediate difference in symptom score following the onset of the exposure to a chemical mixture followed by a decline in the response over the course of the exposure – typical of an odor adaptation response (Figures 2); ii) a difference in symptom score after several hours of exposure – suggestive of a physiological response (Figures 3); and iii) no difference in the symptom score between the chemical exposures and control condition – indicating that the chemical exposures did not affect the symptom being evaluated (Figures 4). The figures provided for each response type are examples of that response type. The figures for all of the symptoms are given in the supplementary data.

Adaptation Response

The following symptoms and environmental quality ratings, which were statistically different during exposures to simulated bioeffluents and/or short chain carbonyls and acids compared to the control condition, displayed a trend consistent with an adaptation response: odor intensity (Figure 2), air freshness, air quality, and nose irritation. Throat irritation has a similar trend but the differences were not statistically different. These symptoms and ratings of environmental quality are most likely driven by an odor perception or responses of the nasal or pharynx passages. This temporal pattern is consistent with odor perception often having an adaptation character, i.e. a diminishing response for a continuous stimulus.⁵³ Air quality and nose or throat irritation are linked to odors perceived in the air.

Physiological Response

A number of symptoms did not change immediately after the introduction of the simulated bioeffluents or the short chain carbonyls/organic acids into the CEF, even though they could be smelled at that time. Rather, symptom scores became statistically different from the control sessions one to three hours after the onset of the exposure. Once these symptom reports increased, they remained elevated during the remainder of the exposure. Thus, the participant did not “adapt” or “habituate” to the effects of the chemical agent. These symptoms can be broadly categorized into three response types: ocular irritation (eye irritation (Figure 3), eyes smarting, eyes aching), dryness (lips dry, eyes dry, mouth dry, very thirsty) and general well-being (severe headache, nose blocked, dizzy, claustrophobic) and a single environmental parameter (noise level). These symptom reports indicate that ocular irritation, measures of dryness and some general well-being symptoms take time to develop following the onset of exposure and persist while the exposure is present. Thus, they are not solely driven by a response to an odor but likely represent physiological responses to the chemical exposures. After the subjects returned to the clinic, the symptom scores were not significantly different from the baseline questionnaire, except for “eyes dry” for the simulated bioeffluent exposure. This indicates that the symptoms reported were transitory. However, qualitative differences are suggested in the plots of two of the general well-being symptoms in the clinic post exposure – severe headache and dizziness. That is, these symptoms remained somewhat elevated even after subjects returned to the clinic following the exposure period in the CEF.

Although we would not expect the CO₂ concentrations generated in our indoor environment to be of sufficient magnitude to cause or contribute to the persistent symptoms observed such as headache and dizziness, previous studies have shown that controlled exposure to CO₂ at 1000 ppm resulted in reduced decision making performance relative to a background concentration of 600 ppm.¹³ Furthermore, other studies have documented similar symptoms as those observed in the present study in response to CO₂ exposure and other bioeffluent compounds may have a role in causing these symptoms.^{13, 54, 55}

The occurrence of persistent symptoms, upon exposure to certain chemicals within an aircraft environment, warrants further examination across a wider range of subjects, including those that might be more responsive to chemical exposures than the healthy, young females participants studied.

No Effect

Many of the symptoms and environmental qualities were either not different or had only a single time point that was statistically different between the chemical exposures and the control session. (A difference at a single time point could be random effect due to multiple comparisons and not a true change in symptom scores.) This indicates that exposures to the compounds at the concentrations used in this study did not affect these symptoms. These included: physical parameters related to the environment (thermal environment (Figure 4), too bright, too noisy, thermal sensation, air too dry), external measures of dryness (skin dry, nose dry), and some general well-being conditions (sleepy, interested, tired, uptight or frustrated, jittery). Some of these symptom scores and environmental qualities varied little

over the entire time the subjects were in the simulated aircraft cabin while the scores for other symptoms changed in a similar manner but were independent of the exposure. This might be expected when an individual is in an enclosed, confined environment for an extended period of time where she cannot control her physical surroundings. Most of these symptoms have not been reported in the literature to be altered by chemical exposures. The lack of an association between many symptoms and chemical exposures provides a validation that the subjects did not report a generalized increase of all symptoms regardless of the exposure mixture, symptom type, or odor. Instead, there appeared to be some specificity of response influenced by specific chemical exposures (i.e., simulated bioeffluents, short chain carbonyls/organic acids) with some responses independent of the presence of an odor.

Overall, the subjects reported statistically significant differences in their perception of odor and air quality, as well as symptoms of nose and throat irritation, immediately after the simulated bioeffluent and short chain carbonyls/organic acids were introduced into the air of the simulated cabin compared to control sessions. These symptoms and environmental qualities are consistent with the most prevalent and highest intensity symptoms and perceptions of the environment reported from inflight research.^{4,56–59} While the intensity of the response decreased over the course of the exposure, the symptom ratings did not return to those originally reported at baseline conditions until the participants were no longer exposed to these compounds. One to three hours after initiating exposures to either simulated bioeffluents or short chain carbonyls/organic acids, symptoms related to ocular irritation, dryness and general well-being (particularly headache) were reported to be more pronounced compared to the control session. These symptoms persisted at elevated response levels throughout the exposure, with some residual effects still present after the subjects returned to the clinic room for their debriefing questionnaires.

Since all of the subjects used in this study were healthy, young female adults, it is not known whether the reported symptoms would be more or less serious in men, in individuals that might have underlying health conditions or those more susceptible to chemical exposures (those with chemical sensitivities). Further, while the compounds and concentrations were selected based on what is likely to be present in aircraft cabins, there is a range of concentrations and other compounds present in the cabin air not included in this study. The same compounds are likely to be in other enclosed and indoor settings, though potentially at different concentrations depending on the occupant density, the ventilation rate and infiltration of ozone. Thus, the role of these compounds in affecting indoor air quality needs consideration and greater attention needs to be directed to the specific compounds that are part of bioeffluent particularly in settings with high density of people such as transportation vehicles, class rooms, conference rooms and auditoriums and/or low air exchange rates such as homes and buildings.

Conclusions

Our study results affirm that some specific classes of chemicals (e.g., short chain organic acids and carbonyls and sulfurous compounds) present in aircraft cabins can contribute to the complaints reported by passengers to include not only negative perceptions of air quality

but also persistent symptoms. The role of exposure to bioeffluent compounds to cause symptoms in environmental settings that have high density of people and/or low air exchange has not been well studied. While the symptoms reported were not of a magnitude to need medical intervention and generally did not result in persistent health effects following termination of the exposure in the healthy subjects that participated in this study, they are detectable during the time of exposure which was created to simulate actual air travel. The subjects in this study were young, healthy, women from a university community and not representative of the general population of individuals who use commercial aircraft. While many people will have little or no response to chemicals within the aircraft cabin, a greater response to the compounds found in cabin air than identified in this controlled experiment may be manifested by the subpopulation of the general public who use air transportation and have compromised health conditions that make them susceptible to exposures to chemicals that can cause irritation or other health symptoms. The results clearly indicate differential responses to chemicals commonly found indoors. Filtration that targets the most offending of these chemical groups has the potential to improve perceptions of air quality and to reduce symptoms commonly reported among individuals who spend extended time in both aircraft cabins and other enclosed settings. The regulations that set requirements for outside ventilation in an aircraft (FAR 25.831(a)) and CO₂ (FAR 25.831(b2)) should consider if the FAR regulations provide a comfortable environment for the traveling public. This finding should also be considered when defining the indoor air quality based on ASHRAE Standard 62.1-2013 Guideline for indoor building environments which are also based on CO₂ levels.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Practical Implications

Transitory symptoms reported while flying can result from exposure to volatile organic compounds in the cabin air. Bioeffluents, compounds emitted from people, include irritating compounds that can contribute to those symptom reports, as do one- or two-carbon carbonyls and organic acids which have multiple sources in aircraft cabins. Current ventilation regulations that influence air quality within an aircraft may not be adequate to prevent these transitory symptoms in healthy adults and may not be protective for susceptible individuals. The health symptom effects of these compounds should also be considered in other indoor and enclosed settings when evaluating air quality.

Figure 1.
Controlled Environmental Facility with three rows of aircraft seating.

Figure 2.

Temporal changes in perception of environmental quality score for odor intensity for each of the four conditions.

Symbol represents the mean and the bar $\pm$ one standard error.

Scale range is measured as 0cm – 2.8cm: 0 corresponds to “no odor” and 2.8 corresponds to “overpowering odor”.

Figure 3. Temporal changes in symptom score for eye irritation for each of the four conditions. Symbol represents the mean and the bar $\pm$ one standard error. Scale range is measured as 0cm – 2.8cm: 0 corresponds to “no irritation” and 2.8 corresponds to “overpowering irritation”.

Figure 4. Temporal changes in symptom score for temperature of the environment for each of the four conditions. Symbol represents the mean and the bar $\pm$ one standard error. Scale range is measured as 0 corresponds to “clear acceptable” and 6.7 corresponds to “clearly unacceptable”.

Table 1

Compounds Selected for the Exposures in the Controlled Environmental Facility (CEF), Concentrations Measured in Aircraft Cabins and Target Chamber Concentrations

Compounds	Airplane Conc. ^{15, 18, 21–29, 31, 56}	Proposed Chamber Conc.	Comments: Odor thresholds vary widely across individual and within the reported literature. Source of Odor Threshold Values: ^{60, 61}
Longer-chain carbonyls:			
Hexanal	3.1 ppb mean, 0.1–12 ppb	5 ppb	Surrogate for pentanal and hexanal Odor Threshold 14ppb No effects reported below 1ppm
Nonanal	2.8 ppb mean, 0.5–8 ppb	10 ppb	Surrogate for heptanal – octanal Odor Threshold 2.2 ppb Produced from reactions between ozone and certain unsaturated hydrocarbons (e.g., oleic acid)
Decanal	2.2 ppb mean, 0.5–7 ppb	6 ppb	Odor Threshold 0.9 ppb Produced from reactions between ozone and certain unsaturated hydrocarbons (e.g., skin oil constituents)
Trans 2-Octenal	0.2 ppb mean, 0.05–0.5 ppb	0.6 ppb	Surrogate for heptenal Odor Threshold 2ppb Emitted by people – contributes to body odor – and produced by ozone chemistry
Trans 2-Nonenal	0.3 ppb mean, 0.1–0.6 ppb	0.6 ppb	Odor Threshold 2ppb Emitted by people – contributes to body odor – and produced by ozone chemistry
Benzaldehyde	2.3 ppb mean, 0.2–5 ppb	2 ppb	Odor Threshold 40 ppb Occupational TWA 2ppm Produced from reaction between ozone and styrene; other sources
Simulated Bioeffluents			
Phenol	Not Available	10 ppb	Has been measured in indoor air at levels between 5 and 10 ppb. Occupational Threshold Limit Value (TLV) is 5 ppm
Dimethyl sulfide	0.4 ppb	1 ppb	Odor Threshold 2.5 ppb Occupational Threshold Limit Value (TLV) 10ppm
Ethyl mercaptan	Not available; estimated 0.7 – 1.1*	1 ppb	Odor Threshold 0.8ppb Occupational TLV 0.5ppm Emitted by people – contributes to body odor). Steady-state concentration calculated using published metabolic generation rate
Propyl mercaptan	Not available; estimated 0.6–0.9*	1 ppb	Emitted by people – contributes to body odor). Expected to be similar to ethyl mercaptan but threshold data not available. Steady-state concentration calculated using published metabolic generation rate.
Org. acids & short carbonyls			
Formaldehyde	7 ppb mean, 3–26 ppb	10 ppb	Odor Threshold 1ppm NIOSH TLV 16ppb (carcinogen) OSHATWA 750ppb
Acetaldehyde	5 ppb mean, 2–20 ppb	35 ppb	Odor Threshold 0.07 ppm NIOSH not listed - carcinogen OSHA 200 ppm

Compounds	Airplane Conc. ^{15, 18, 21–29, 31, 56}	Proposed Chamber Conc.	Comments: Odor thresholds vary widely across individual and within the reported literature. Source of Odor Threshold Values: ^{60, 61}
Acrolein	0.5 ppb mean, 0.1–9 ppb	8 ppb	Odor Threshold 0.03ppm Occupational TWA 0.1ppm
Butenal		5 ppb	Odor Threshold 0.5ppm Occupational TLV 0.3ppm
Formic acid	3 ppb mean, 0.6–8 ppb	12 ppb	Surrogate for acetic acid (10 ppb) Odor Threshold 21ppm Occupational TWA 5ppm
Pyruvic acid	Not available	3 ppb	Metabolic and fermentation product Steady-state concentration calculated using published metabolic generation rate
Butanoic acid	Not available	3 ppb	Odor Threshold 3.9ppb Steady-state concentration calculated using published metabolic generation rate
Pentanoic Acid	Not available	3 ppb	Odor Threshold 4.8ppb. Bioeffluents and plane engine emissions; estimated to be similar to butanoic acid, the four carbon analog of this 5 carbon compound
Caprylic acid	Not available	3 ppb	Odor Threshold 8ppb Degradation product of skin oil Steady-state concentration calculated using published metabolic generation rate

Table 2

Demographics of Study Participants

Age (years)	18–25	25–35	>35	
	40	4	0	
Ethnicity	White	Black	Asian	Hispanic
14	7	21	2	

Table 3
Mean Concentrations ($\mu\text{g}/\text{m}^3$) Measured in Air in the CEF when Subjects Were Present

Group	Compound	Molecular Wt	Target Concentration in CEF ppb	Target Concentration in CEF $\mu\text{g}/\text{m}^3$	Measured + Concentration ($\mu\text{g}/\text{m}^3$) During Long Chain Carbonyls Injection	Measured+ Concentration ($\mu\text{g}/\text{m}^3$) During bioeffluents Injection	Measured+ Concentration ($\mu\text{g}/\text{m}^3$) During Short Chain Carbonyls and Acids Injection	Measured+ Concentration ($\mu\text{g}/\text{m}^3$) During Control Condition
1	Hexanal	100.2	5	20.5	14	<2	<2	<2
1	Nonanal	142.2	10	58.3	54	<2	<2	<2
1	Decanal	156.3	6	38.4	28	<2	<2	<2
1	Trans 2-Octenal	126.2	0.6	3.1	2.6	<2	<2	<2
1	Trans 2-Nonenal	140.0	0.6	3.4	2.2	<2	<2	<2
1	Benzaldehyde	106.1	2	8.7	9.7	<2	<2	<2
2	Phenol	94.1	10	38.6	<2	59	<2	<2
2	Dimethyl sulfide	62.1	1	2.5	<2	<2	<2	<2
2	Ethyl mercaptan	62.1	1	2.5	<2	7 *	<2	<2
2	Propyl mercaptan	76.2	1	3.1	<2	7 *	<2	<2
3	Formaldehyde	30.3	10	12.4	<10	<10	17	<10
3	Acetaldehyde	44.1	35	63.2	<10	<10	90	<10
3	Acrolein	56.1	8	18.4	<5	<5	15	<5
3	Butenal	70.1	5	14.4	ND	ND	ND	ND
3	Formic acid	46.0	12	22.6	#	#	#	#
3	Pyruvic acid	88.1	3	10.8	<2	<2	25	<2
3	Butanoic acid	88.1	3	10.8	<2	<2	11	<2

* ethyl and propyl combined

† Concentrations were averaged across all five groups of subjects for the indicated exposure condition.

ND No standards for the DNPH derivatives of butenal

Formic acid blank was contaminated so air concentration could not be determined

Means (SDs) of scores for selected symptoms and their changes from baseline along with p-values indicating differences between exposures and control condition for 36 subjects. See Table S1 for additional symptoms.

Table 4

Symptom Time ^	Control	Bio-effluents#	p-value* F-test	Short Chain#	p-value* F-test	Long Chain#	p-value* F-test
Air quality							
Baseline	0.93 (0.64)	1.05 (0.47)	.20	1.10 (0.50)	.06	1.01 (0.53)	.38
5 hours	1.01 (0.48)	0.59 (0.76)	.0014	0.73 (0.63)	.03	0.95 (0.46)	.66
7 hours	1.02 (0.51)	0.54 (0.67)	<.0001	0.68 (0.64)	.0039	1.03 (0.40)	.97
Change from baseline	0.08 (0.57)	-0.46 (0.85)	.0012	-0.37 (0.68)	.0068	-0.07 (0.61)	.35
Change from baseline	0.09 (0.45)	-0.51 (0.79)	<.0001	-0.42 (0.64)	.0003	0.02 (0.43)	.60
Eye Irritation							
Baseline	0.18 (0.17)	0.14 (0.14)	.064	0.14 (0.14)	.13	0.19 (0.18)	.83
5 hours	0.15 (0.14)	0.29 (0.36)	.0067	0.24 (0.42)	.077	0.24 (0.31)	.098
7 hours	0.15 (0.14)	0.24 (0.31)	.056	0.25 (0.38)	.092	0.20 (0.22)	.32
Change from baseline	-0.03 (0.11)	0.15 (0.31)	.0010	0.09 (0.37)	.021	0.05 (0.22)	.16
Change from baseline	-0.03 (0.14)	0.11 (0.25)	.0087	0.11 (0.35)	.0081	0.01 (0.16)	.39
Nose Irritation							
Baseline	0.19 (0.27)	0.20 (0.35)	.98	0.15 (0.15)	.33	0.18 (0.20)	.77
5 hours	0.18 (0.19)	0.33 (0.37)	.0074	0.27 (0.37)	.094	0.22 (0.29)	.55
7 hours	0.15 (0.17)	0.33 (0.41)	.0055	0.29 (0.43)	.038	0.21 (0.24)	.34
Change from Baseline	-0.02 (0.17)	0.13 (0.34)	.027	0.12 (0.35)	.045	0.03 (0.23)	.47
Change from Baseline	-0.04 (0.25)	0.14 (0.37)	.027	0.14 (0.43)	.027	0.03 (0.20)	.38
Throat Irritation							
Baseline	.018 (0.24)	0.15 (0.15)	.49	0.21 (0.31)	.53	0.17 (0.18)	.93
5 hours	0.16 (0.18)	0.24 (0.29)	.082	0.23 (0.34)	.17	0.18 (0.22)	.72
7 hours	0.16 (0.18)	0.21 (0.22)	.33	0.22 (0.32)	.21	0.18 (0.16)	.81
Change from Baseline	-0.02 (0.14)	0.10 (0.29)	.036	0.02 (0.32)	.46	0.00 (0.18)	.70
Change from Baseline	-0.01 (0.15)	0.06 (0.24)	.19	0.02 (0.35)	.58	0.00 (0.16)	.81

		Control	Bio-effluents [#]	p-value [*] F-test	Short Chain [#]	p-value [*] F-test	Long Chain [#]	p-value [*] F-test
Symptom Time[^]								
Nose Blocked								
Baseline		1.18 (1.48)	1.31 (1.37)	.5585	1.25 (1.47)	.73	1.19 (1.49)	.92
5 hours		1.20 (1.49)	2.35 (2.09)	.0017	1.51 (2.00)	.38	1.66 (1.80)	.23
7 hours		1.23 (1.59)	2.14 (2.01)	.0015	1.68 (1.91)	.11	1.44 (1.49)	.53
Change from Baseline		0.06 (1.28)	1.04 (1.81)	.0051	0.27 (1.68)	.55	0.47 (1.45)	.25
Change from Baseline		0.09 (1.16)	0.83 (1.61)	.017	0.44 (1.97)	.26	0.36 (1.08)	.41
Nose Running/Dry								
Baseline		3.91 (1.87)	3.97 (1.64)	.87	3.81 (2.06)	.77	3.79 (1.70)	.75
5 hours		4.31 (1.77)	4.18 (1.85)	.77	3.98 (2.16)	.42	4.12 (1.70)	.66
7 hours		3.79 (2.08)	3.87 (1.89)	.84	4.13 (2.09)	.38	3.52 (2.09)	.47
Change from Baseline		0.31 (1.35)	0.21 (2.11)	.8184	0.17 (1.88)	.75	0.31 (1.50)	.99
Change from Baseline		-0.01 (1.50)	-0.10 (2.19)	.8538	0.32 (2.11)	.47	-0.27 (1.91)	.58
Mouth Dry								
Baseline		1.90 (1.92)	2.03 (1.99)	.67	1.72 (1.77)	.59	1.63 (1.87)	.50
5 hours		1.83 (1.89)	2.72 (2.31)	.015	1.98 (2.09)	.68	2.14 (2.06)	.36
7 hours		1.62 (1.77)	2.81 (2.25)	.0020	2.31 (2.30)	.0708	1.82 (1.97)	.54
Change from Baseline		-0.06 (1.83)	0.63 (1.93)	.11	0.26 (2.32)	.46	0.52 (1.94)	.20
Change from Baseline		-0.28 (1.29)	0.78 (2.06)	.015	0.59 (2.08)	.047	0.20 (1.95)	.28
Lips Dry								
Baseline		2.18 (2.06)	1.88 (1.98)	.29	1.89 (2.00)	.30	1.66 (1.80)	.12
5 hours		1.94 (1.93)	2.90 (2.37)	.0045	2.23 (2.18)	.38	2.19 (1.92)	.38
7 hours		2.13 (1.90)	2.73 (2.30)	.10	2.53 (2.29)	.28	1.98 (2.09)	.763
Change from Baseline		-0.24 (1.81)	1.03 (2.20)	.0005	0.34 (1.65)	.10	0.54 (1.22)	.029
Change from Baseline		-0.05 (1.30)	0.85 (1.92)	.013	0.64 (1.94)	.056	0.32 (1.31)	.32
Skin Dry								
Baseline		2.26 (2.29)	2.32 (2.07)	.82	2.23 (2.15)	.94	1.60 (1.78)	.048
5 hours		1.94 (1.99)	2.63 (2.04)	.035	2.46 (2.14)	.11	1.84 (1.80)	.90
7 hours		2.14 (2.03)	2.44 (2.13)	.38	2.42 (2.00)	.42	1.71 (1.74)	.24

See Table S1 for additional symptoms.

For symptoms (irritation, nose blockage, dryness): Severity of symptoms increases as value decreases from 6.7 cm to 0 cm; for perception of environmental quality (Air Quality; thermal environment; air movement, noise level): Higher ratings indicate greater symptom or perception severity.