Malodor from Industrial Hog Operations, Stress, Negative Mood, and Secretory Immune Function in Nearby Residents

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ABSTRACT

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(Under the direction of Steve Wing)

In North Carolina, and throughout the United States, pork production has industrialized over the last 20 years, with the majority of hogs now raised in confinement houses and their waste stored either beneath the confinement houses or in open-air lagoons until it is sprayed via irrigation systems on nearby fields as fertilizer. People living near these industrial farms report frequent exposure to malodor and adverse effects on their health and quality of life. Evaluated here is the hypothesis that malodor is an environmental stressor that, when appraised as such, exerts an immunosuppressive effect on secretory immune function in neighbors.

Seventy-one study participants in eastern North Carolina collected data twice daily for approximately 2 weeks. They reported the intensity of malodor from the hog operation(s) on a 9-point scale where 0 = no odor and 8 = extreme odor. They also rated feelings of stress/annoyance, anxiety, unhappiness, anger, and confusion on the same 9-point scale, and collected whole, unstimulated saliva samples for secretory immunoglobulin A (sIgA) analysis. Data were analyzed using multilevel models, appropriate for analysis of longitudinal data. Reported stress and negative mood appeared to be associated with malodor; odds ratios for a 1-unit change on the odor scale ranged from 1.4 to 1.7. The

effects of malodor, stress, and mood on sIgA secretion were mixed; they did not appear to have an overall effect on sIgA, though there was some evidence of an effect in particular subgroups of the study population. Malodor from industrial hog operations does appear to affect stress and negative mood in neighbors, but sIgA may not be a useful marker of its physiologic effect.

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ABBREVIATIONS

IHO(s)	Industrial hog operation(s)
CAFO(s)	Confined animal feeding operation(s)
sIgA	Secretory immunoglobulin A
CHEIHO	Community Health Effects of Industrial Hog Operations
JHAC	John Henryism Active Coping

CHAPTER 1

INTRODUCTION

In 1985, North Carolina ranked 15th in the United States in hog production [1]. By 1998, North Carolina had moved to 2nd, where it remains, ranked behind the state of Iowa [1, 2]. In North Carolina, the average hog inventory on any given day is approximately 10 million hogs [3]. With increased industrialization of hog production, the number of hog farms decreased dramatically, while the number of hogs per farm increased [1]. Recent data indicate that over 95% of the total number of hogs raised in NC were produced in facilities of at least 2000 animals each, and 75% were produced in facilities of at least 5000 animals each. Only one-tenth of one percent (0.1%) was raised on farms of less than 100 animals each [4].

In North Carolina, airborne emissions (including odorants) from industrial hog operations (IHOs) are complex mixtures of gases and dusts from confinement houses, waste lagoons, and spray fields. The confinement houses are significant sources of organic dusts, onto which odorants adsorb [5], and endotoxins from dander, feed, and dried feces. Ammonia and hydrogen sulfide from decomposing animal waste are also released [6]. Fans vent this mixture out of the confinement houses and into the surrounding environment. Waste lagoons hold tons of feces and urine, which anaerobically decompose releasing ammonia, hydrogen sulfide, and volatile organic compounds into the air [6]. In order to prevent overflow, waste is pumped from the lagoons and sprayed on adjacent fields as

fertilizer. Thus, waste is aerosolized, enabling it and concomitant odorants to travel with wind to more distant locations. Furthermore, lagoon breaches and over-spraying of waste contribute to pollution of surface waters adjacent to lagoons and spray fields.

People of color and people in poverty bear a disproportionate share of the burden associated with large-scale hog production. Wing *et al* analyzed the location and population characteristics of 2,514 hog operations in North Carolina [1] and found that block groups in the highest quintile of poverty had seven times as many hog operations as those in the lowest quintile of poverty, adjusted for population density. Furthermore, there were five times as many operations in the highest three quintiles of percent non-white compared to the lowest, adjusted for population density. Similar results were found in an analysis of the racial and socioeconomic characteristics of North Carolina middle schools located near IHOs [7]. On average, schools with higher white enrollment (> 63%) and lower poverty (< 47% of students receiving subsidized lunches) were located twice as far from IHOs, relative to lower white/higher poverty schools (10.8 miles vs 4.9 miles).

Health effects documented in neighbors of IHOs

Although many occupational and human challenge studies have shown that dusts, gases and pathogens inside hog confinement houses can affect the health and respiratory function of workers and naïve volunteers [8-23], less is known about the health effects in neighbors. The growing literature on neighbors includes several surveys of physical health symptoms. The earliest survey [24], conducted in Iowa, identified symptoms reported in

excess by participants living within 2 miles of an IHO, compared to demographically comparable controls. The authors grouped the symptoms into the following 4 clusters: (1) respiratory symptoms, (2) nausea, weakness, dizziness, and fainting, (3) headaches and plugged ears, and (4) burning eyes, runny nose and throat. In North Carolina, a similar survey [25] was conducted in three rural communities, one within 2 miles of an IHO, one within 2 miles of a cattle operation, and a third community at least 2 miles from any livestock operation utilizing a lagoon waste management system. Participants living near the hog operation reported more frequent headaches, runny nose, sore throat, excessive coughing, diarrhea, and burning eyes than did residents of the community with no intensive livestock operations. A second survey conducted in North Carolina [26] documented higher frequencies of the same sets of symptoms reported by neighbors of IHOs, relative to frequencies reported by controls.

Several studies have documented effects of odor from IHOs on psychological health, mood, and quality of life. Bullers [26] found higher mean scores on a short form of the CES-D depression scale in neighbors than in controls (2.24 vs 1.84). Though this short form performed reliably, the novel use/scoring of a 7-item short form limits the comparability of the above scores to those reported in other studies. The survey conducted in Iowa, however, did not find differences in symptoms of depression, measured by the Zung Self-Rating Depression Scale [24]. Schiffman et al [27] evaluated effects of hog odor on mood; 44 adults living near IHOs completed Profile of Mood States (POMS) questionnaires on each of 4 days when odors were present, while 44 matched controls completed the questionnaire on each of 2 days. POMS scores were higher in neighbors, who reported more tension, depression, anger, fatigue, confusion, and less vigor.

Wing and Wolf [25] assessed effects on quality of life, determined by asking how often neighbors of hog operations could open windows or go outside during nice weather. By that metric, residents reported greatly reduced quality of life relative to residents of the other two communities. Researchers in northern Germany conducted a cross-sectional survey [28] of the prevalence of odor from confined animal feeding operations (CAFOs, predominantly swine and poultry), odor annoyance, and quality of life (QoL), assessed by the Short Form 12 Health Survey (SF-12). They found that average scores on the SF-12 decreased with increasing levels of reported odor annoyance. However, in noting that, "Better risk communication might improve QoL in concerned neighbors of intensive livestock production facilities [28]", they appear to consider the odor a nuisance but not a public health problem.

There are several limitations to the existing studies of the health effects in neighbors of IHOs described above. None has included incidence data; all existing studies use prevalence data. Health outcomes have been assessed through self-report, which can be useful but subject to recall bias. (It is, however, important to note that the studies by Thu et al [24] and Wing and Wolf [25] included symptoms not expected to be associated with exposure to airborne emissions from IHOs in order to assess whether neighbors of IHOs uniformly over-reported symptoms relative to controls. Neither study found evidence of over-reporting by neighbors, who did not report 'dummy' symptoms more frequently than controls.) Exposure to airborne emissions from IHOs has been assessed either by residential proximity or by self-reported odor. Residential proximity is non-specific; self-reported odor is not an objective measure of exposure, and the extent to which odor is a proxy for exposure to the airborne pollutants associated with health effects is unknown. Self-report of odor

and/or mood, however, can be useful if one is interested in neighbors' perceptions of odor and/or mental health, for example. An additional limitation is the extent to which the comparison groups serve as adequate controls for the exposed. The literature on health effects in neighbors is growing, and future studies are likely to address the limitations outlined above.

Health effects associated with residential proximity to other polluting industrial facilities

A group of Canadian scientists examined the psychosocial effects of residential proximity to 3 solid waste facilities in southern Ontario (1 municipal solid waste incinerator and 2 municipal solid waste landfills; one was accepting waste at the time of the study and the other was a new landfill under construction not yet accepting waste) [29-31]. The study was both quantitative and qualitative. Quantitative data were collected via a phone survey of stratified random samples of residents who lived at varying distances from the facilities, defined by zones. Residents were asked about quality of life, attitudes towards neighborhood or home, social networks, and psychosocial health and well-being, measured by the 20-item General Health Questionnaire (GHQ) and the somatic complaints subscale of the Symptom Check List - 90 (SCL-90). [29] Qualitative data were collected through interviews with a subset of residents from the quantitative study, focus groups with members of community groups/organizations, discussion groups comprised of subsets of interview participants, textual analysis of media coverage, and social network analysis. [29]

Outcome variables were (a) how concerned residents were about the facility in their neighborhood, (b) whether such concern was health-related, and (c) whether they had taken

any action if concerned. The authors concluded that concern was well explained by a combination of variables reflecting characteristics of the individual (age, gender, etc.), the exposure (site, distance from site), social network membership, and general health status, while action was primarily a function of social network membership. The variables with significant effects varied from model to model, which prevented drawing more specific conclusions. [30]

Of particular relevance here are the results of the in-depth interviews with residents living near the facilities [31]. Many of the concerns expressed in interviews were similar to those expressed by neighbors of industrial hog operations. Neighbors of the solid waste incinerator expressed concern about stack emissions and odors, about respiratory problems that they attributed to the stack emissions, about water pollution and property values. Neighbors of the active landfill were concerned about traffic and pests (seagulls), which prevented them from enjoying the outdoors and from hanging clothes outside to dry. They also mentioned concern about odors, property values, and noise. Neighbors of the landfill under construction expressed concern about water quality, traffic, property values, and pests (seagulls and rodents), and expressed distrust of authorities who assured them that they did not need to worry about adverse effects of the landfill. [31]

The above-mentioned research group [29-31] also conducted a study of the effects residential proximity to a petroleum refinery in Oakville, Ontario [32]. They examined changes in odor perception, odor annoyance, and symptoms (for example, cough, nausea, and headache) before and after the refinery implemented an odor reduction plan. Like exposure to airborne emissions from industrial hog operations, residential exposure to refinery emissions was described as involuntary and uncontrollable, with similar uncertainly among

the public and the scientific community about exposures and potential health effects. Community health surveys were conducted in 1992 and 1997; residents responded to questions about symptoms, chronic illness, mental health, exposure to indoor air pollution, attitudes and beliefs about the community and the refinery, and beliefs about health effects of refinery emissions. The authors noted that the symptom questions were asked early in the survey prior to questions about the refinery, presumably to avoid the implication that symptoms were due to refinery exposures. Proxy exposure to refinery emissions was determined by dividing residents into 3 zones based on their distance from the refinery, history of odor complaints, distance from other odor sources, and prevailing wind direction. [32]

Frequency of odor perception and odor annoyance appeared to decrease after the odor reduction plan was implemented by the refinery, though people living closest to the refinery continued to report more frequent odor perception and annoyance than those living further away. Symptom prevalences were similar in 1992 and 1997 and did not appear to be consistently affected by residential proximity to the refinery. For approximately one-third of the symptoms reported in 1992, there appeared to be some evidence of increased symptom rates in those living closest to the refinery relative to those living farthest, but precision is modest. There appeared to be evidence of increased symptom rates for fewer symptoms in 1997, though again, results were imprecise. Reported symptom rates were, however, clearly higher among people reporting more frequent odor perception and annoyance (with odds ratios as large as 4.1). Because symptom rates were more strongly associated with odor perception than with distance to the refinery, the authors concluded that symptoms were likely odor-mediated. [32]

In another qualitative study, 29 in-depth interviews were conducted with residents living near the refinery [33]. Again, concerns were similar to those expressed by neighbors of industrial hog operations. They reflected on times when odor interrupted backyard barbecues and when refinery deposits appeared on cars and doorknobs. They expressed the desire to be able to raise their children in a small town with fresh air. Residents who noticed that odors had improved after abatement still expressed concern about odorless emissions. Others expressed concern about perceived clusters of excess cancers, about property values, and about being unfairly dumped on. They expressed distrust of corporations and government and the influence of money. Like CAFO neighbors, neighbors of the refinery employ similar strategies to cope with odors, including closing windows, keeping the house closed up, and staying indoors. [33]

In an effort to understand symptom reporting "at levels insufficient to cause acute or even subacute symptoms by known toxicologic mechanisms", the California Department of Health Services conducted surveys of frequency/severity of symptoms, frequency of odor perception, and degree of environmental worry among residents who lived near 3 hazardous waste sites in southern California (acid petroleum sludge; municipal and sewage waste, paint and petroleum sludge; residues from synthetic rubber manufacturing, DDT) [34]. Residents were informed that the department was conducting a study of "environmental health issues"; the hazardous waste sites were not mentioned explicitly.

Odds ratios for symptom reports in people who expressed a high degree of environmental worry versus no environmental worry ranged from 5.3 to 11.9. For people who reported frequent odor versus those who reported no odor, odds ratios ranged from 4.2 to 5.6. There appeared to be positive interaction between odor and worry; odds ratios for

people with a high degree of worry who reported frequent odor versus those who were not worried and reported no odor ranged from 12.0 to 38.1. The study authors offered several potential explanations for the presence of acute symptoms in neighbors of hazardous waste sites: (1) an acute toxicologic response to pollutants from the facility, considered rare given the infrequency of exposures at levels capable of producing a toxicologic response; (2) an odor-mediated response, "innate odor aversions, exacerbation of underlying medical conditions, and conditioned responses to odors after traumatic chemical overexposures"; and (3) a stress-mediated response in which odor triggers symptoms via stress or activation of the autonomic nervous system in people characterized by environmental worry. [34]

A second article, published by the same authors of the above-mentioned study in the same issue of Environmental Health Perspectives, explores a number of hypotheses to explain higher symptom prevalences around hazardous waste sites [35]. The article references 5 studies conducted or supervised by the California Department of Health Services, 3 of which were reviewed above. Residents living near the 5 sites were concerned about perceived increases in birth defects and cancers, but the research conducted did not find evidence of elevated rates. The studies did, however, find elevated rates of a number of symptoms. The hypotheses explored were: (a) a classical toxicological reaction, (b) an immunological or other physiogenic "hazardous waste syndrome", (c) behavioral sensitization, (d) a psychosomatic reaction to stress, (e) mass psychogenic illness, and (f) reporting bias.

Neutra et al [35] excluded (a) as a possible explanation because exposures were believed to be at low part per billion levels and (e) because the pattern of symptom reporting did not meet the definition for mass psychogenic illness. They considered (b) possible,

though unlikely. Behavioral sensitization (i.e., symptoms triggered at low-levels of exposure following sensitization after a high-level exposure) was also possible but unlikely because few, if any, community residents had been previously exposed at high levels.

The authors concluded that some combination of reporting bias and an odor-worry-stress process was the most likely explanation of increased symptom reporting by neighbors of hazardous waste sites. Reporting bias could occur if people concerned about their proximity to a waste site were more likely to recall or report symptoms, or had a lower threshold for noticing symptoms, than people who were not concerned about their proximity or who did not live near a hazardous waste site. Three of the 5 studies included toothache in the list of symptoms in order to evaluate over-reporting; toothache was reported in excess in 2 of the 3 studies. [35]

Another survey of symptoms conducted by the California Department of Health Services documented higher symptom rates prior to an announced community-wide aerial pesticide application than after the aerial application, an effect consistent with stress and/or anxiety. With the exception of the aforementioned study before and after an aerial pesticide application (which did not address odor), people who reported odor from the various hazardous waste sites were more likely to report symptoms. Even within zones of similar odor (as proxies for chemical exposures), those who reported odor also reported more symptoms. [35]

Health Effects Associated with Other (Non-Odor) Environmental Stressors

Loud noise, like odor, is also an environmental stressor whose effect on health is hypothesized to be stress-mediated. Frenzilli et al suggest involvement of the pituitary-adrenocortical axis and investigated cellular effects of noise stress in the laboratory setting, specifically, the effect of noise on damage to the rat adrenal gland DNA [36]. They exposed rats to 12 hours of 100 db(A) noise (likened to that of a car horn, trombone, or disco) and sacrificed the rats either immediately or 24 hours after the cessation of exposure. They observed significantly increased DNA damage, compared to controls, in both groups. Davies et al investigated the effects of occupational noise on mortality from acute myocardial infarction [37]. They described the potential stress-mediated effect of noise on cardiovascular disease as follows:

> It is hypothesized that the normally transient physiological stress responses to noise of the sympathetic nervous and neuroendocrine systems become pathogenic when chronically or repeatedly activated. Thus, temporary increases in blood pressure might, through structural autoregulation, lead to permanent elevations and then hypertension; repeated oversecretion of cortisol in response to noise exposure may lead to visceral fat accumulation and to insulin resistance.

The authors used noise dosimetry data and work histories to calculate exposures to noise among a cohort of lumber mill workers in British Columbia, Canada. For the full cohort, standardized mortality ratios (SMR) for acute myocardial infarction were elevated for exposure thresholds > 95 db(A) for 20+ years (SMR_{20-29}=1.2 [0.9-1.5] and SMR_{29+}=1.3 [0.9-1.8]). For the subgroup of workers employed before hearing protection use was common, the ratios were elevated for thresholds > 90 db(A) for 10+ years (SMR_{10-19}=1.3 [1.0-1.6] and SMR_{19+}=1.4 [1.0-2.0]). When restricting follow-up time to working years only, ratios were further elevated; SMRs ranged from 1.8 [1.0-3.3] for 3-9 years of exposure to 2.7 [1.4-4.9] for 19+ years of exposure. [37]

In a study of the effect of traffic noise on the risk of incident myocardial infarction in Berlin, Germany, Babisch et al [38] used city noise maps to calculate a traffic noise level for each study participant's home; cases and hospital-based controls were recruited prospectively from 32 hospitals. Study participants provided information on potential confounding factors via interview and rated the extent to which they were annoyed/disturbed by traffic noise at home on a 5-point scale. For both men and women, mean annoyance scores increased with increasing estimated noise exposure. For men, the adjusted odds ratio for an estimated noise exposure > 70 db(A), compared to ≤ 60 db(A), was 1.3; in the subset who had lived in their homes for at least 10 years, the odds ratio was 1.8. There did not appear to be an effect of traffic noise exposure on myocardial infarction in women. [38]

Conceptual framework

Shusterman, in his "Critical Review: The Health Significance of Environmental Odor Pollution", synthesizes the work that he and others have done on the health effects of exposure to environmental odors [39]. He divides potential explanatory mechanisms into two classes: toxicologic (i.e., classical physiological responses to irritants and pathogens present in airborne plumes) and non-toxicologic (i.e., psychophysiological responses to odor). Chemical analysis of air pollution from hog facilities suggests that the concentrations of constituents of the odor plume emanating from confinement houses and lagoons tend to be lower than those at which irritant effects are expected to occur [40]. The occurrence of symptoms, reviewed above, at presumably low levels of exposure suggests a non-toxicologic mechanism [34, 35, 39, 40] (Figure 1 [41]).

To explore potential mechanisms through which odor may affect the health of neighbors, I considered the hypothesis that exposure to noxious odor from industrial hog operations has a stress-mediated effect on the secretory immune system, specifically, that odor as a stressor has an immunosuppressive effect on secretory immunoglobulin A (sIgA). In a recent review of the literature on stress and secretory immunity, Bosch, Ring, *et al* summarize the biological rationale for a potential effect of stress on salivary secretory immune function:

> Salivary glands, as with other mucosal glands, are largely under autonomic nervous system control. The preganglionic autonomic centers in the brain stem that regulate salivary gland activity receive direct inhibitory and excitatory inputs from neural structures in the forebrain that are part of recognized 'stress circuits' and centers for homeostatic regulation. The salivary glands form a highly sophisticated endpoint in the CNS control of local immune defenses, capable of responding instantly and with a high level of specificity to potential source of harm (e.g., stress, inflammation). This remarkable ability, together with their strategic location at the portal of entry to the respiratory and gastrointestinal tract, make these glands ideally suited to provide the host with a first line of defense. [42]

Odor as a stressor

Studies of responses to odorant exposures may be conducted in the laboratory or in the environment. Laboratory exposures differ from environmental exposures. The former typically last several seconds while the latter can last for much longer periods of time. Laboratory odors exist in the vapor phase while environmental odors typically include odorants in both particulate and vapor phases; laboratory odors tend to be more temporally stable. Laboratory experiments enroll healthy subjects while people exposed environmentally include both the healthy and unhealthy; they also typically consider few

health endpoints, most frequently whether the odorant produces an olfactory or trigeminal response. [43]

Laboratory studies

Laboratory research on sensory responses to odor separates its odorant properties (stimulating the olfactory nerve) from its irritant properties (stimulating the trigeminal nerve). Much of the work is focused on the assessment of the irritancy properties of volatile chemicals, such as acetone or isopropanol, in order to set occupational exposure limits [44-47]. As such, it seeks to distinguish between objectively measured irritation and that which is subjectively reported [47], further exploring how odor perception and characteristics of the individual affect self-reports of irritation [46]. Dalton concludes, "Negative findings on objective measures of irritation that cannot be reconciled with subjective reports occurring at much lower levels of exposure should prompt a careful investigation into the other factors (e.g., cognitive or emotional) that may be modulating the sensory response" [46].

Lateralization is frequently used to objectively assess the irritant properties of an odorant chemical. If the chemical is indeed an irritant and is presented at a concentration above its irritancy threshold, then the research subject can identify whether the chemical is being presented to the right nostril or the left nostril; if the chemical is merely an odorant, s/he cannot distinguish between the nostrils. [46, 48] Dalton et al use phenylethyl alcohol as a negative control for reported irritation. It is a volatile chemical with odorant, but not irritant, properties. The extent to which research subjects report irritation following phenylethyl alcohol exposure is considered reporting bias and adjusted for in the analysis.

The combination of results from laboratory assessments of odor perception, perception of irritation in response to index and control chemical exposures, and measurement of objective signs of irritation inform comments on the appropriate selection of occupational exposure limits (for example, [44, 45, 48, 49]).

Of greater interest to an investigation of the health effects associated with exposure to odor from industrial hog farms via an odor-worry-stress process is the literature on the relationships between odor, annoyance, and/or health symptoms and the extent to which the relationships are modified or affected by cognitive and/or personality factors. "Annoyance" appears to be used more commonly than "stress" in the research on responses to odor as an environmental stressor. It is defined as a sort of global marker of "discomfort summarizing different aspects… such as nuisance, disturbance, and unpleasantness" [50] and elsewhere as "a feeling of displeasure associated with any agent or condition believed to affect adversely an individual or a group" [51, 52].

In the laboratory setting, Seeber et al conducted a series of experiments in which research subjects were exposed to 1 of 14 odorant chemicals over the course of 4 hours; chemical concentrations were constant in some experiments and fluctuating in others. Prior to the experiment, subjects completed the trait form of the state-trait-anxiety inventory; they rated odor, irritation, and annoyance up to 9 times during the 4-hour experiment. The authors observed strong positive correlations between chemical concentration and odor, irritation, and annoyance. Odor was more strongly correlated with annoyance than was irritation; though the authors concluded that trait anxiety (high vs. low) did not modify the relationship between odor and annoyance, the data appear to suggest that people classified as high anxiety reported more annoyance than those classified as low (not statistically significant). [50]

Winneke et al conducted a two-part study in which citizens of Dusseldorf, Germany who lived near either traffic noise or industrial odors completed a questionnaire that assessed annoyance and were then categorized as high or low responders; a subgroup then participated in a laboratory experiment in which they were exposed to controlled levels of traffic noise, hydrogen sulfide (H_2S), and environmental tobacco smoke that varied over the course of 1 hour. The authors observed that reported annoyance increased as the levels of noise, H_2S, and smoke increased, though there appeared to be some adaptation to odor (H_2S) over time. Furthermore, subjects classified as high responders reported more annoyance in response to all exposures than did low responders. [53]

Asmus and Bell conducted an experiment in which 240 undergraduate students were randomly assigned to 1 of 5 odor conditions (4 malodors and 1 non-odor condition). Prior to the experiment, they measured trait coping using the COPE scale and informed subjects that exposures were not harmful or toxic (of interest below). The authors operationalized negative affect as the degree of discomfort subjects experienced while exposed, drawing from older research which "observed that 'uncomfortable' and 'unpleasant' [as descriptors of exposure] were especially predictive measures in studying environmental stress" [54]. Odor predicted negative affect, but the relationship was not modified by coping style. (The authors reported that the odor×coping interaction term was not significant but did not include the data.) [54]

Consistent with the data reported by Shusterman et al [34] and Neutra et al [35] from the symptom surveys conducted in California, Dalton et al have observed that what subjects believe about their exposures can affect how they report odor intensity, irritation, and health symptoms [45]. Ninety research subjects were divided into 3 groups and given a positive,

negative, or neutral bias towards the odorant chemicals to which they were exposed. Those given a positive bias reported lower odor intensities, less irritation, and fewer symptoms; the negative/neutral bias groups were more similar, with the neutral bias group reporting the highest symptom ratings. The authors hypothesized that no information about the consequences of exposures could produce more anxiety/concern than having presumably truthful information about negative consequences (which, in this case, were purportedly long-term). [45]

Field studies

Steinheider and Winneke [52] present data from one of a series of studies that informed the Guideline on Odour in Ambient Air in Germany, a directive that limits the frequency of environmental odor exposures based on odor-annoyance research [55]. They emphasize the importance of accurate assessment of environmental odor for regulatory purposes, given large inter-individual differences in reported odors and annoyance responses. In a later article, Sucker et al contrast the measurement of noise and odor, two common environmental stressors; noise is more easily objectively measured (in db(A)), whereas the measurement of odor is made difficult by (a) the chemical complexity of the odor plume, (b) properties of the odor source, terrain, and weather, and (c) its perception and appraisal by the exposed individual [56].

This research group developed an exposure assessment tool in which a team of trained odor observers semi-randomly visited a network of observation points around an industrial odor source and noted the presence or absence of odor every 10 seconds for 10

minutes [52]. If odor was present for a total of at least 1 minute, then that hour counted as an "odor hour"; the total number of odor hours was divided by the number of hours per year to calculate a % odor-hours/year. Individuals living near observation points completed questionnaires on demographic variables, odor annoyance ("To what extent are you disturbed/annoyed by industrial odors?"), perceived health, and coping style. Steinheider and Winneke observed positive associations between odor prevalence and annoyance. They did not observe modification of the effect by age or perceived health status; they did, however, observe modification by problem-oriented coping (related to perceived control), with stronger associations between odor prevalence and annoyance in people with high problem-oriented coping scores. [52]

The German Guideline on Odour in Ambient Air codified the odor assessment tool, with requirements that the network of monitoring points encircle the industrial source within a radius of 30 times the stack height and that assessment occur for at least 6 months in both cold and warm weather. The Guideline limits odor exposures to 10 % odor-hours/year in residential areas and to 15 % odor-hours/year for industrial areas. Both et al reported results from a 2004 study in which trained odor observers added intensity and hedonic tone to their assessments. Pleasant odors were, as expected, much less annoying than neutral or unpleasant odors. They concluded that odor intensity had "no additional influence" on the relationship between odor frequency and annoyance (i.e., did not change the beta coefficient for odor frequency when odor intensity was added to the model). [55] However, the lack of temporal specificity between the assessments of odor and assessments of annoyance suggests it difficult to link changes in odor intensity to greater or lesser degrees of annoyance.

Secretory Immunoglobulin A and the Mucosal Immune System

Secretory immunoglobulin A (sIgA), the primary salivary immunoglobulin, is also the predominant immunoglobulin in "external secretions of the gastrointestinal, respiratory, and genitourinary tracts and of the lacrimal and mammary glands." [57] It functions as a first line of defense against pathogens invading via the mucosal epithelia, particularly pathogens "borne in aerosols, the environment, and the diet" [58]. The average synthesis rate of sIgA is 66 mg/kg of body weight/day, approximately two-thirds of which is produced in mucosal lymphoid tissue [59]. In contrast, the average rates of secretion (in mg/kg/day) for the other antibody types are: 34 for IgG, 7.9 for IgM, 0.4 for IgD, and 0.02 for IgE. IgA is also found in serum, though at much lower concentrations relative to other antibody types and relative to its levels in secretions. [60]

Serum and secretory IgA exist in distinct molecular forms; in serum, IgA is predominantly monomeric, while secretory IgA is predominantly polymeric. Polymeric IgA (pIgA) usually exists as a dimer, two monomers linked by a polypeptide J chain, though some tetramers are found as well. [57] The high proportion of polymeric IgA in secretions is due to two factors. First, receptors on mucosal epithelial cells are specific for polymeric IgA, and polymeric IgA is therefore selectively transported into the secretory lumen. During transport, a glycoprotein known as the secretory component is linked to one of the monomeric units and protects pIgA from degradation by proteolytic enzymes [60]. The high proportion of pIgA in secretions is also due to local synthesis by plasma cells committed to IgA production in mucosal tissues, which are separated by a basement membrane from

circulating antibodies. Local production of secretory IgA is advantageous in that sIgA secretion can be regulated locally according to physiological need. [58]

Polymeric IgA has 2 antigen-binding sites per monomeric unit, that is, 4 antigen-binding sites per dimer, 8 sites per tetramer, etc. and therefore a relatively high affinity for binding antigen [61]. Though the specific mechanisms are uncertain, research suggests that IgA might protect against infection in several ways. It may bind antigen and prevent its attachment to the mucosal epithelium, thereby preventing the entrance of antigen into the epithelial layer of the mucosal surface [59]. IgA may also combine with antigens and other particles in the mucosal lumen, creating larger aggregate particles, thus slowing movement to the surface of the mucosal epithelium. The actual elimination of pathogens may be nonspecific. [58] "By reducing the motility of microorganisms and preventing their adherence to the epithelial surface, IgA would render them susceptible to the natural cleansing function of the mucosae" [58]. Two additional functions of IgA include viral neutralization and antigen clearance from the blood [59, 60]. Several epidemiologic studies have suggested that sIgA plays a role in preventing infection in both adults and children [62-64], though others have not been able to establish such a link.

Stress and Secretory Immunity

In their review of the literature on stress and secretory immunity, Bosch et al observe that the effects of stress on sIgA levels are best understood by categorizing the stressor according to whether it is acute or chronic in duration. Many authors have studied the effects of stress associated with academic exams, though some have examined sIgA levels in

conjunction with a single examination while others have examined sIgA levels during an extended examination period. Bosch et al report that the former acute single examination stressor appears to be associated with increased sIgA, while the latter extended period stressor appears to be associated with decreased secretion. Studies of chronic stress measured using inventories of major life events or minor daily hassles tend to be associated with decreased sIgA. Acute naturalistic stressors tended to be associated with increased sIgA. [42]

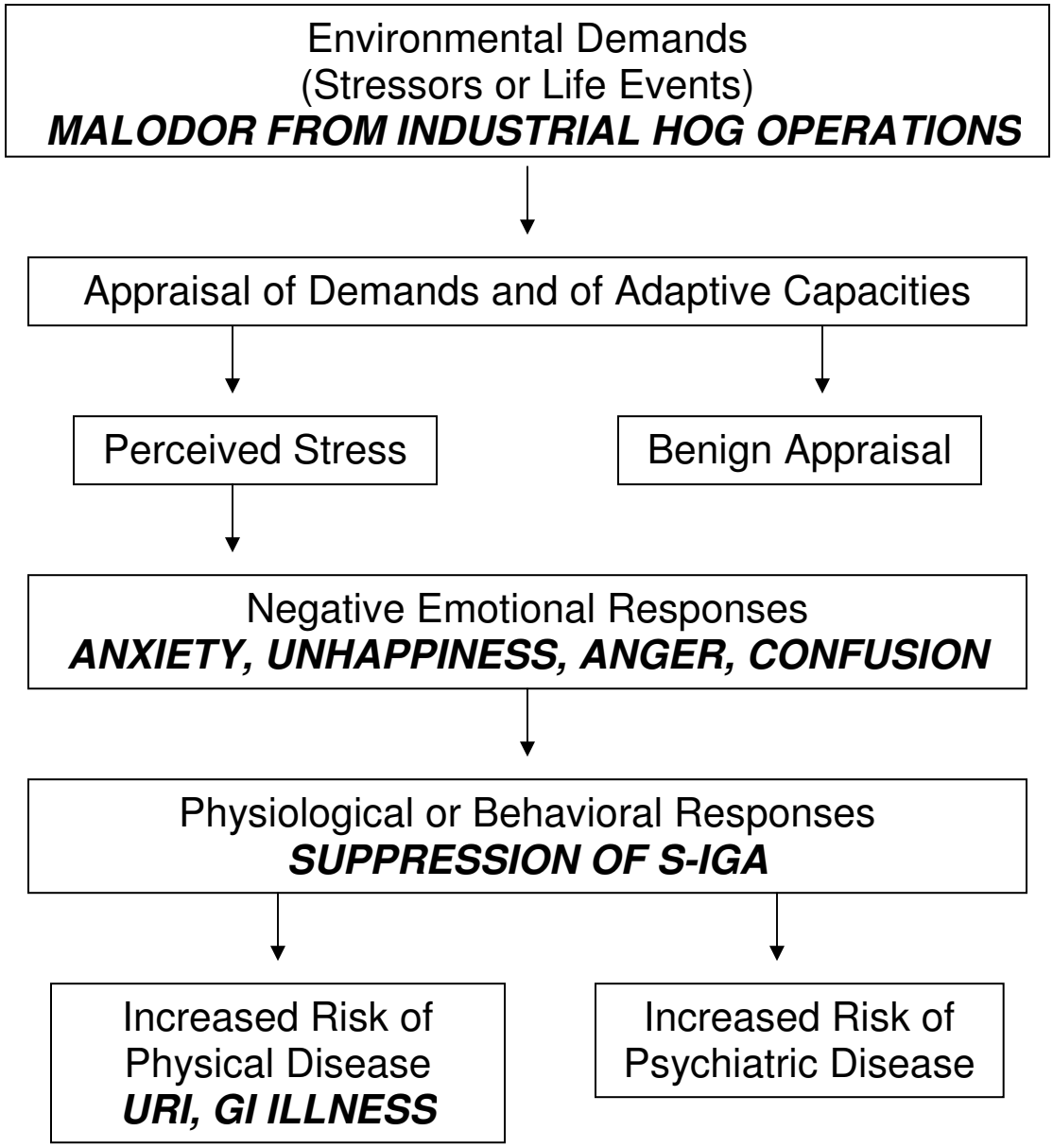
Numerous studies have been conducted in which volunteers are asked to undergo a series of laboratory stressors, and considerable work has been done to understand the timing of the sIgA response to stress in the laboratory setting. [42] The timing of the response remains to be resolved. However, the fact that the response occurs on the order of minutes, rather than hours, suggests an effect of stress on the release of sIgA from stored reserves or an effect on the translocation of sIgA across the mucosal epithelium, rather that an effect of stress on the production of sIgA [65]. Laboratory stressors are acute in duration and have generally been associated with increased sIgA levels, although stressors that are associated with a passive coping response (for example, cold pressor [66, 67] or viewing a surgical video [68]) tend to suggest decreased sIgA. Bosch et al note that the data on sIgA effects of acute duration laboratory stressors might be better understood by classifying the stressors according to the type of autonomic nervous system response they elicit. [42]

As mentioned previously, I considered the hypothesis that exposure to noxious odor from industrial hog operations has a stress-mediated effect on the secretory immune system (sIgA). The nature of hog odor as a stressor is rather unique in the literature on stress and secretory immunity, particularly when compared to the laboratory setting in which the effects

of stress on sIgA have typically been examined. It is a chronic stressor that occurs in repeated acute episodes; people exposed cannot escape and cannot predict exposure. Animal and human studies suggest that the psychophysiologic impacts of stress can be greater when stressors are unpredictable and uncontrollable [68-70]. Furthermore, exposure to hog odor occurs at home, not in the laboratory. Even an experiment designed to evaluate the effects of an unpredictable and/or inescapable stressor in the laboratory setting is still unable to capture the psychological and physiological impact of being exposed at home. Nonetheless, that both (a) chronic stressors and (b) acute laboratory stressors associated with a passive coping response tend to be associated with decreased sIgA secretion suggests that any sIgA response to hog odor might be immunosuppressive as well.

With respect to the conceptual framework outlined in Figure 1, I will note that I am not trying to draw a direct link between decreased sIgA levels and an increased risk of infection, though it may be possible; the results on sIgA and infection are equivocal, and the decreased sIgA levels found in our previous study are still within normal range [71]. The relationship between odor and stress is reasonably grounded in the literature. I aim to extend that literature by examining a relationship between odor and stress in another context – in residents involuntarily exposed to hog odor in and around their homes. I have further chosen to evaluate sIgA as a marker of a physiological response (see Figure 1) to odor as an environmental stressor.

Figure 1.1*



* Adapted from Cohen, S., R. Kessler, and L. Gordon, *Strategies for measuring stress in studies of psychiatric and physical disorders*, in *Measuring Stress: A Guide for Health and Social Scientists*, S. Cohen, R. Kessler, and L. Gordon, Editors. 1997, Oxford University Press: New York.

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CHAPTER 2

DESIGN AND METHODS

Specific Aims

Specific Aim #1: to determine whether exposure to odor from industrial hog operations is perceived as stressful by persons exposed to the odor in and around their homes and whether any such association is modified by age, gender, coping style, or threshold odor sensitivity.

Specific Aim #2: to determine whether stress reported after exposure to hog odor is associated with decreased secretion of salivary secretory IgA and whether any such association is modified by age, gender, or coping style.

Specific Aim #3: to determine whether exposure to moderate to high reported levels of odor is associated with decreased secretion of salivary secretory IgA and whether any such association is modified by age, gender, coping style, or threshold odor sensitivity.

Overview

The Community Health Effects of Industrial Hog Operations (CHEIHO) study was a collaborative community based participatory research project, incorporating both quantitative and qualitative data collection. Study participants were recruited in clusters, or neighborhoods. At a central location in each cluster, research staff set up a monitoring trailer to collect data on coarse and fine particulate matter, semi-volatile particulate matter, endotoxin, hydrogen sulfide, and weather. Data were downloaded weekly. Prior to commencement of data collection, study participants attended a training session where they learned to complete the required data collection activities and were tested for innate sensitivity to odor using butanol standards.

Study participants collected data at their homes twice daily for two weeks. Each morning and evening, at least one hour after eating, drinking, or brushing teeth, they spent 10 minutes outdoors; they then provided odor ratings and saliva samples, reported on stress, mood, and physical health symptoms, and measured blood pressure and lung function. Research staff members reviewed the data at the end of the first week and collected all materials after the second week. Prior to completion of the 2-week study period, participants also completed a questionnaire, providing information on their homes, occupations, existing health problems, medication use, quality of life, and coping style using the John Henryism Active Coping scale. Following completion of the study period, they filled out a short exit questionnaire and completed the Pearlin mastery scale.

Participant recruitment.

Eligible participants were non-smoking adults who lived within 1.5 miles of at least one industrial hog operation who volunteered to complete data collection activities twice daily for two weeks and with freezer space to store saliva samples. Multiple adults per household were eligible to participate. Study participants were recruited through a number of community organizations operating in eastern North Carolina. Members of the community organizations talked with exposed individuals about the project and gave them a copy of the study brochure (see Appendix 1) for their perusal. Once several interested individuals were identified, a meeting was set up, and members of the CHEIHO project staff introduced the project, provided details on the data collection process, and answered questions. CHEIHO staff then completed an eligibility questionnaire by phone.

Participant Training.

All eligible participants attended a 3-hour training session on the evening before they began to collect data. CHEIHO staff first reviewed the consent form and answered any questions about the project. Study participants consented to participate and further agreed not to reveal their participation to others outside the project in order to protect the confidentiality of their neighbors who had also elected to participate with them. Project staff then trained participants in each activity they were to complete each subsequent morning and evening. They practiced completing the pages of the data collection diary, collecting saliva samples, taking blood pressures, and testing lung function. Participants were given the

opportunity to practice all pieces of the data collection process until they could do so comfortably.

At the training session, each participant was tested for innate sensitivity to odor using butanol standards. S/he was asked to smell the contents of up to 12 pairs of bottles in series and asked to state whether the odor from the first or second of the pair was stronger. One member of the pair contained 15 mL of deionized water, and the other contained 15 mL of a butanol/water solution. The concentration of butanol in solution increased two-fold in each successive pair from 10 ppm to 20480 ppm. The order in which the two bottles were presented to the study participant was random. S/he was presented pairs until s/he correctly identified the butanol odor five times in a row. The concentration of butanol in the first of the five pairs, the lowest of the five, was the participant's threshold odor sensitivity. [1]

Exposure Assessment.

The exposure metric of primary importance to the previously listed specific aims was the rating of the presence/intensity of perceived hog odor. While spending 10 minutes outdoors, participants rated any odor they recalled for each hour since they last collected data (previous morning or evening). They used a 9-point scale, where 0 = no odor and 8 = very strong odor, and noted where they were when they noticed the odor, at home outside, at home inside, or not at home (Figure 2.1). After returning indoors, they rated the odor for the 10-minute period on the same 9-point scale.

There are other methods for characterizing the intensity of odor. Schiffman et al used several in their quantification of odorant chemicals from several industrial hog operations in

North Carolina. They collected air samples in Tedlar® bags, which were transported back to their laboratory where trained odor panelists rated the intensity of odor. In the field, participants used Scentometers (Barnebey and Sutcliffe, Columbus, OH) to determine odor intensities. The device has 6 inlets, opened one at a time, which permit progressively decreasing amounts of odorous air to enter a mixing chamber where it is diluted with clean air; the intensity of the odor is measured in dilutions to threshold, the factor by which the odorous air must be diluted to render the odor undetectable (below threshold). A third method required participants to rate odor intensity by selecting 1 of a series of 12 bottles of butanol (concentrations ranged from 10 to 20,480 ppm) whose intensity most closely matched the intensity of the hog odor they smelled at their homes. [2]

Odor intensity rated on a 9-point scale by study participants is the least precise method but the one most feasible for twice daily data collection at home. It would not have been feasible to collect bag samples twice daily for 2 weeks from multiple study participants who were collecting data at the same time. Furthermore, Schiffman et al found that the particulate fraction of the odor plume adhered to the Tedlar® bags, and therefore the intensity of the odor was reduced relative to that measured in the field [2]. We considered using Scentometers but found them too difficult to use and consequently too difficult to train study participants to use without the presence of a member of the CHEIHO staff. We did not consider using the butanol bottles for daily odor ratings.

Other exposure data collected by the CHEIHO project, analyzed elsewhere, included the following odor plume constituents: coarse particles, > 2.5 µm and < 10 µm in aerodynamic diameter and collected on filters; endotoxin, a cell wall component of gram negative bacteria [3], measured on the same filters; PM_{10}, < 10 µm in aerodynamic diameter

and measured in real time; semi-volatile PM_{10}, collected at $4^{o}C$ in real time to capture particles that would volatilize at higher temperatures; and hydrogen sulfide, a toxic gas produced when lagoon waste decomposes, measured over a range of < 2 – 90 parts per billion. Data on temperature, humidity, dewpoint, rainfall, and wind direction were also collected because they can affect pollutant transport. All monitoring equipment was mounted to a farm trailer and moved from community to community throughout the project (see photograph in Appendix 2).

Outcome Assessment.

Irritation. After spending 10 minutes outside and rating the presence/intensity of hog odor, study participants indicated whether they experienced irritation of the eyes, nose, throat, or skin or coughing while outside. They were permitted to check all that apply.

Mood. The questionnaire then asked a series of mood questions: "How do you feel now? Stressed or annoyed? Nervous or anxious? Gloomy, blue, or unhappy? Angry, grouchy, or bad-tempered? Confused or unable to concentrate?" They responded using a 9-point scale where 0 = not at all and 8 = extremely. The "Stressed or annoyed?" question was an ad-hoc single item measure designed to determine whether the participant perceived stress or annoyance after exposure to hog odor, an attempt to assess primary appraisal in which environmental demands are deemed either irrelevant, benign-positive, or stressful (Figure 1.1).[4] The other 4 questions were from 4 of the 6 sub-scales of the Profile of Mood States instrument, reflecting the Tension-Anxiety, Depression-Dejection, Anger-Hostility, and

Confusion-Bewilderment mood states. Questions from the Fatigue and Vigor sub-scales were not used. (This was one of a series of decisions made in an effort to reduce the burden of data collection on study participants. The Fatigue and Vigor sub-scales were deemed the least pertinent of the 6 sub-scales.)

Physical symptoms. Participants were asked if they had a cough, difficulty breathing, wheezing or whistling, runny nose, irritation or burning of the nose, mucus or phlegm, sore throat, burning eyes, itching eyes, poor appetite, nausea, diarrhea, headache or have felt light-headed or dizzy in the hours since the previous morning or evening data collection activities. They were also asked about symptoms not expected to be associated with exposure to odor or pollution from hog operations (chest tightness, bleeding gums, trouble hearing, back ache, fever, aching or painful joints) in order to assess whether participants discriminated between symptoms in reporting the presence or intensity of symptoms when odors were strong. Of particular interest to Specific Aims #2 and #3, participants were asked if they suffered a cold, flu, or stomach flu because such illnesses could produce an immune response that could affect the interpretation of the data on salivary secretory IgA. Participants used the same 9-point scale used to answer questions about mood, where 0 = not at all and 8 = extreme.

Secretory IgA. Participants collected 2-minute unstimulated whole saliva samples into pre-weighed collection tubes and stored samples in their freezers. Samples were transferred on dry ice to the lab at the EPA Human Studies Facility on the UNC campus and stored at -20 degrees Celsius until the tubes were weighed again. The mass of the saliva was determined, then its volume, assuming a specific gravity of 1 g/mL. Salivary flow rates were calculated

by dividing the saliva volume by the 2 minute collection time. Samples were stored at -80 degrees Celsius until they were sent by overnight mail on dry ice to Salimetrics, LLC in State College, PA for sIgA analysis. Salimetrics, LLC ran the samples in duplicate by enzyme-linked immunosorbent assay (ELISA) and included quality controls in each assay. Duplicate sIgA concentrations (µg/mL) and their average were returned to UNC in an Excel spreadsheet. sIgA secretion rates (µg/min) were determined by multiplying the concentrations by the salivary flow rates [5].

Though not analyzed here, participants took their blood pressure with an automatic blood pressure monitor that reported systolic and diastolic blood pressures and pulse rate. They also blew into an AirWatch Asthma Monitor (iMetrikus, Inc.) that measured peak expiratory flow (L/min) and forced expiratory volume in the first second (L). A photograph of all of the equipment that participants used to collect data is in Appendix 3.

Modifier Assessment. Gender and age were questions asked on the eligibility questionnaire. Threshold odor sensitivity was assessed using the previously described butanol standards. Coping style was assessed via the 7-item Pearlin Mastery Scale and the 12-item John Henryism Active Coping Scale [6-8]. Pearlin and Schooler consider mastery a facet of one's psychological coping resources, that persons with a high sense of mastery are better able "to perceptually control the meaning of experience in a manner that neutralizes its problematic character." [6] Samples items include the following statements, to which participants responded by selecting 1 of 5 response categories that ranged from "strongly agree" to

"strongly disagree": "There is really no way I can solve some of the problems I have" and "I can do just about anything I really set my mind to."

The John Henryism Active Coping (JHAC) scale was developed by Sherman James in the early 1980's as a measure of "the degree to which [black Americans] felt they could control their environment through hard work and determination" [8]. He hypothesized a poorer health outcome (higher blood pressure) in men who scored high on the scale but lacked the resources to control their environments [8]. Dressler et al re-state the hypothesis elsewhere – in sum, that striving in the face of severe constraints takes a toll on one's health [9].

Because the scale was developed in a black American population in eastern North Carolina, we thought it particularly applicable to our predominantly black study population of neighbors of IHOs in eastern NC. Sample items from the JHAC scale include the following, to which participants responded by selecting 1 of 5 responses that ranged from "completely true" to "completely false": "I've always felt that I could make of my life pretty much what I wanted to make of it", "Once I make up my mind to do something, I stay with it until the job is completely done", and "When things don't go the way I want them to, that just makes me work even harder". [8]

Consent and Confidentiality. The CHEIHO study was approved annually by the Institutional Review Board of the University of North Carolina at Chapel Hill. CHEIHO staff implemented several measures to protect the identity and identifying information of all study participants. Each participant was assigned a study number, and that number was used, instead of names, on all materials the participant completed. All paper files were stored in

locked file cabinets, and all data sets containing participant data were password protected. In the informed consent process, study participants agreed not to reveal the names of other members of their communities that had also chosen to participate with them in the research study. As an additional layer of protection, CHEIHO obtained a Certificate of Confidentiality from the U.S. Department of Health and Human Services, which protects identifying information even under court order or subpoena. Institutional Review Board approval was also obtained for the analyses conducted in Chapters 3 and 4.

Data entry and data cleaning. All monitoring data were transferred to the project programmer for data cleaning. All participant data recorded in journals were entered in Visual FoxPro 6.0. A 10% random sample of all journals was re-entered to determine the rate of data entry errors. The programmer ran data checks on all journal data and flagged questionable and missing data points. Flagged data was re-checked for data entry errors. Errors made by study participants were either corrected or set to missing. For example, on several occasions participants incorrectly recorded in their data collection journals the 5-digit identification number printed on their saliva collection tubes. (The identification number linked a particular tube to the date/time it was collected.) If the correct tube number could be determined from the list of tube numbers assigned to that participant, then the number recorded in their journal was corrected; otherwise it was set to missing.

Statistical Analysis

As stated above, each study participant collected data twice daily for two weeks, and exposure to odor varied over the 2-week period of data collection. Thus, each participant

was both exposed and unexposed to odor over time and served as his/her own control. Potential confounders were time-dependent covariates, factors associated temporally with both exposure and outcome. Time independent factors, such as age or gender, were not evaluated as confounders because their association with exposure and outcome did not vary over the 2-week period of data collection.

Data analysis began with an analysis of missing data; missing data were not imputed because proportions missing were ≤ approximately 5%. I conducted univariate analyses to assess cutpoints for categorical variables and to assess the normality of continuous variables. I then conducted stratified analyses, though such analyses did not take into account the correlated structure of the data. In order to account for the fact that each participant served as his/her own control, I transformed the outcome variables by subtracting each person's mean value from all of his/her observations (for example, subtracted the mean sIgA concentration for person X from all 28 sIgA concentrations) and used the transformed variables in additional stratified analyses.

For the modeling stage of the analysis, I used multilevel models because such models take into account the correlated structure of the nested and longitudinal data. There were three levels in the multilevel model: time (within person), person (within community), and community. Typical epidemiologic models estimate some average intercept and average slope for the effect of the exposure of interest on the outcome, or a transformation of the outcome (a logit transformation in logistic regression, for example). Hierarchical models permit both the intercept and the slope estimated for each person to vary around the overall averages. These models can estimate both fixed effects (analogous to the effects estimated in typical epidemiologic models) and random effects, those effects that are permitted to vary

between persons. All variables included as random effects were also included as fixed (average of the random effects) effects in the model.

General Model Form

The general model form is detailed below. It contains a random intercept component, in which the intercept is permitted to vary between community and between person within community in order to account for the repeated measurements made on individuals and for the clustering of individuals in communities. Additionally, it includes a random slope component, in which the effect of variable 2 on the outcome is permitted to vary between community and between person within community.

Level 1:

$Y_{ijk} = \beta_{0jk} + \beta_1 variable1 + \beta_{2jk} variable2 + r_{ijk}$; $r_{ijk} \sim N(0,\sigma^2)$

where Y_{ijk} is the outcome measurement on person j in cluster k at timepoint i

k^{th} cluster: k = 1, 2, 3, … 16
jk^{th} person: jk = 1, 2, 3, … 71
i^{th} timepoint: i = 1, 2, 3, … i

outcome for the i^{th} measurement in the jk^{th} individual =
person specific intercept (β_{0jk}) + variable1 (β_1) + person specific variable2 (β_{2jk}) + residual within person variation (r_{ijk})

Level 2:

$\beta_{0jk} = \gamma_{00} + \gamma_{01} community_k + \gamma_{02} person_j(community_k) + \mu_{0jk}$; $\mu_{0jk} \sim N(0,\tau_{00})$

person-specific intercept (β_{0jk}) = mean of person-specific means for outcome (γ_{00}) + contribution from $community_k$ (γ_{01}) + contribution from $person_j$ in $community_k$ (γ_{02}) + residual between person variation (μ_{0jk})

$\beta_{2jk} = \gamma_{20} + \gamma_{21} community_k + \gamma_{22} person_j(community_k) + \mu_{2jk}$; $\mu_{2jk} \sim N(0,\tau_{22})$

person-specific slope for variable2 effect (β_{2jk}) = mean of person-specific effects of variable2 (average effect of variable2) (γ_{20}) + contribution from $community_k$ (change in variable2

effect by community$_k$) (γ_{21}) + contribution from person$_j$ in community$_k$
(change in variable2 effect by person$_j$ within community$_k$) (γ_{22})
+ residual between person variation in slope (μ_{2jk})

Combined equation:

$$Y_{ijk} = \gamma_{00} + \gamma_{01}\text{community}_k + \gamma_{02}\text{person}_j(\text{community}_k) + \beta_1\text{variable1} + \gamma_{20}(\text{variable2}) + \gamma_{21}(\text{community}_k)(\text{variable2}) + \gamma_{22}\text{person}_j(\text{community}_k)(\text{variable2}) + \mu_{0jk} + \mu_{2jk} + r_{ijk};$$

$r_{ijk} \sim N(0,\sigma^2)$, $\mu_{0jk} \sim N(0,\tau_{00})$, and $\mu_{2jk} \sim N(0,\tau_{22})$

Lagged Analyses

Because we collected data on recalled exposure to odor from hog CAFOs in the hours preceding the completion of the morning and evening data collection protocol (Figure 2.1), I was able to evaluate the relationship between odor at various lags and stress, mood, and sIgA secretion rate. I calculated average and peak odor ratings for 1-, 2-, 3-, 4-, and 6-hour time windows, up to 12 hours prior to time at which stress/mood were rated and saliva samples collected. Time windows were mutually exclusive and were included as multiple independent variables in the same model. Following are sample Level 1 models for (a) 1-hour windows and (b) 4-hour windows: (Level 2 models remain the same as above.)

(a) Level 1 (Time, Within Person):

$$Y_{ijk} = \beta_{0jk} + \beta_{1jk}(\text{odor}_{t-1}) + \beta_{2jk}(\text{odor}_{t-2}) + \ldots + \beta_{12jk}(\text{odor}_{t-12}) + \beta_{13jk}(\text{time of day}) + r_{ijk}; \quad r_{ijk} \sim N(0,\sigma^2)$$

where β_{1jk} is the effect of odor reported in the hour prior to data collection, β_{2jk} is the effect of odor reported 2 hours prior, … β_{12jk} is the effect of odor reported 12 hours prior, β_{13jk} is the effect of time of day (morning or evening), and r_{ijk} is the residual within person variation.

(b) Level 1 (Time, Within Person):

$$Y_{ijk} = \beta_{0jk} + \beta_{1jk}(\text{odor}_{t-1 \text{ to } t-4}) + \beta_{2jk}(\text{odor}_{t-5 \text{ to } t-8}) + \beta_{3jk}(\text{odor}_{t-9 \text{ to } t-12}) + \beta_{4jk}(\text{time of day}) + r_{ijk}; \quad r_{ijk} \sim N(0,\sigma^2)$$

where β_{1jk} is the effect of average/peak odor reported in the 4 hours prior to data collection, β_{2jk} is the effect of average/peak odor reported 5 to 8 hours prior, β_{3jk} is the effect of

average/peak odor reported 9 to 12 hours prior, and the remaining variables are the same as above.

Because potential relationships between sIgA secretion and non-lagged odor appeared to be nonlinear, I considered additional variable codings for odor in the lagged analyses. I created a threshold linear odor term (0-5=0, 6=1, 7=2, 8=3) for each hour and a binary odor term (0-6=0 and 7-8=1) for 1-, 2-, 3-, 4-, and 6-hour windows using the peak odor reported in each time window.

In evaluating stress and mood as predictors of sIgA secretion, I considered stress and mood reported shortly (i.e., minutes) before saliva sample collection and also considered the effect of stress and mood reported at the previous 2 timepoints. I included the stress/mood variables as linear terms and also as binary terms. An example of the Level 1 model for reported stress follows: (Level 2 models remain the same.)

Level 1 (Time, Within Person):

$$\ln(\text{sIgA secretion rate})_{ijk} = \beta_{0jk} + \beta_{1jk}(\text{stressed}_{t0}) + \beta_{2jk}(\text{stressed}_{t-1}) + \beta_{3jk}(\text{stressed}_{t-2}) + \beta_{4jk}(\text{time of day}) + r_{ijk}; \qquad r_{ijk} \sim N(0,\sigma^2)$$

where β_{1jk} is the effect of reported stress approximately minutes before saliva collection, β_{2jk} is the effect of stress reported approximately 12 hours prior, β_{3jk} is the effect of stress reported approximately 24 hours prior, β_{4jk} is the time of day effect, and r_{ijk} is the residual within-person variation.

To examine potentially influential data points and/or people, I used the influence option available in SAS statistical software version 9.1 (SAS Institute Inc., Cary, NC). I evaluated overall influence via the restricted likelihood distance, influence over the magnitude of the beta coefficients using the D and MDFFITS statistics, and influence over

the precision of the betas using the covariance trace and covariance ratio statistics. The iterative analysis sub-option permitted the evaluation of influence over the covariance parameters via the covariance trace and covariance ratio statistics. Influential data points and/or people were those whose exclusion produced marked changes in the above statistics. [10]

All analyses were restricted to data from study participants with at least one odor rating > 3 on the 0 – 8 scale during the 2-week study period. Given a limited budget for the laboratory analysis of salivary sIgA levels, we excluded study participants with little or no variation in exposure to odor over the course of their study participation. Variables, and variable coding, included in the mixed model analyses for each Specific Aim are summarized in the below tables.

Specific Aim #1: to determine whether exposure to odor from industrial hog operations is perceived as stressful by persons exposed to the odor in and around their homes and whether any such association is modified by age, gender, coping style, or threshold odor sensitivity.

Variable	Construct	Role	Frequency of Measurement	Scale	Potential Coding
10-minute odor	Odor rating after 10 minutes spent outside	Exposure	Twice daily	0 - 8	(a) 0 – 8 (b) 0 = 0 on original scale 1 = 1 or 2 2 = 3, 4, or 5 3 = 6, 7, or 8 (c) 0,1 where 1=any odor
Hourly odor	Odor rating for waking hours of the day	Exposure	Up to 24 times per day	0 – 8	Same as above
Peak odor	Highest hourly odor rating in x hours	Exposure	(Derived from hourly odor)	0 – 8	Same as above
Cumulative odor	Sum of hourly odor ratings in x hours	Exposure	(Derived from hourly odor)		Cutpoints determined from variable distribution
Stress	"Stressed or annoyed?"	Outcome	Twice daily	0 – 8	(a) 0 – 8 (b) 0 = 0 on original scale 1 = 1 or 2 2 = 3, 4, or 5 3 = 6, 7, or 8 (c) 0,1 where 1=any odor
Mood	"Nervous or anxious?" "Gloomy, blue or unhappy?" "Angry, grouchy or bad-tempered?" "Confused, unable to concentrate?"	Outcome	Twice daily	0 – 8	Same as above
Cumulative emotional effect	Sum of scores on above stress and mood items	Outcome	Twice daily		Cutpoints determined from variable distribution
Illness	"Cold or flu?" "Stomach flu?"	Confounder	Twice daily	0 – 8	0,1 where 1 = ill

Time of day	Time of day when data was collected (AM,PM)	Confounder			0 = AM 1 = PM
Day	Day of data collection	Confounder			1 = Day 1 2 = Day 2 ... 14 = Day 14
Gender	Male or female	Modifier	Once		0 = male 1 = female
Age	Age in years	Modifier	Once		0 = ≤ median age 1 = > median age
Coping style	(a) John Henryism Active Coping Scale (b) Pearlin Mastery Scale	Modifier	(a) once (b) once	(a)1-5 (b)1-5	(a) 0 = low John Henryism 1 = high John Henryism (b) 0 = low mastery 1 = high mastery
Threshold odor sensitivity	Lowest level at which person can distinguish butanol from water, ppm	Modifier	Once	10, 20, 40, 80, ... 20480	0 = low sensitivity 1 = high sensitivity

Note: Analyses of categorical outcome variables required the use of nonlinear, as opposed to linear, mixed models.

Specific Aim #2: to determine whether stress reported after exposure to hog odor is associated with decreased secretion of salivary secretory IgA and whether any such association is modified by age, gender, or coping style.

Variable	**Construct**	**Role**	**Frequency of Measurement**	**Scale**	**Potential Coding**
Stress	"Stressed or annoyed?"	Exposure	Twice daily	0 – 8	(a) 0 – 8 (b) 0 = 0 on original scale 1 = 1 or 2 2 = 3, 4, or 5 3 = 6, 7, or 8 (c) 0,1 where 1=any odor

Mood	"Nervous or anxious?" "Gloomy, blue or unhappy?" "Angry, grouchy or bad-tempered?" "Confused, unable to concentrate?"	Exposure	Twice daily	0 – 8	Same as above
Cumulative emotional effect	Sum of scores on above stress and mood items	Exposure	Twice daily		Cutpoints can be determined from variable distribution
sIgA concentration	Secretory IgA concentration* (μg/mL)	Outcome	Twice daily	Ratio	Log transformed
sIgA secretion rate	* adjusted for salivary flow rate (μg/min)	Outcome	Twice daily	Ratio	Log transformed
Illness	"Cold or flu?" "Stomach flu?"	Confounder	Twice daily	0 – 8	0,1 where 1 = ill
Time of day	Time of day when data was collected (AM,PM)	Confounder			0 = AM 1 = PM
Day	Day of data collection	Confounder			1 = Day 1 2 = Day 2 … 14 = Day 14
Gender	Male or female	Modifier	Once		0 = male 1 = female
Age	Age in years	Modifier	Once		0 = ≤ median age 1 = > median age
Coping style	(a) John Henryism Active Coping Scale (b) Pearlin Mastery Scale	Modifier	(a) once (b) twice	(a)1-5 (b)1-5	(a) 0 = low John Henryism 1 = high John Henryism (b) 0 = low mastery 1 = high mastery

Specific Aim #3: to determine whether exposure to moderate to high reported levels of odor is associated with decreased secretion of salivary secretory IgA and whether any such association is modified by age, gender, coping style, or threshold odor sensitivity.

Variable	Construct	Role	Frequency of Measurement	Scale	Potential Coding
10-minute odor	Odor rating after 10 minutes spent outside	Exposure	Twice daily	0 - 8	(a) 0 – 8 (b) 0 = 0 on original scale 1 = 1 or 2 2 = 3, 4, or 5 3 = 6, 7, or 8 (c) 0,1 where 1=any odor
Hourly odor	Odor rating for waking hours of the day	Exposure	Up to 24 times per day	0 – 8	Same as above
Peak odor	Highest hourly odor rating in x hours	Exposure	(Derived from hourly odor)	0 – 8	Same as above
Cumulative odor	Sum of hourly odor ratings in x hours	Exposure	(Derived from hourly odor)		Cutpoints can be determined from variable distribution
sIgA concentration	Secretory IgA concentration* (µg/mL)	Outcome	Twice daily	Ratio	Log transformed
sIgA secretion rate	* adjusted for salivary flow rate (µg/min)	Outcome	Twice daily	Ratio	Log transformed
Illness	"Cold or flu?" "Stomach flu?"	Confounder	Twice daily	0 – 8	0,1 where 1 = ill
Time of day	Time of day when data was collected (AM,PM)	Confounder			0 = AM 1 = PM

Day	Day of data collection	Confounder			1 = Day 1 2 = Day 2 … 14 = Day 14
Gender	Male or female	Modifier	Once		0 = male 1 = female
Age	Age in years	Modifier	Once		0 = ≤ median age 1 = > median age
Coping style	(a) John Henryism Active Coping Scale (b) Pearlin Mastery Scale	Modifier	(a) once (b) twice	(a)1-5 (b)1-5	(a) 0 = low John Henryism 1 = high John Henryism (b) 0 = low mastery 1 = high mastery
Threshold odor sensitivity	Lowest level at which person can distinguish butanol from water, ppm	Modifier	Once	10, 20, 40, 80, … 20480	0 = low sensitivity 1 = high sensitivity

Figure 2.1

Day 1: _____ **MORNING** Date: |___|___| 2004 ☐ No data collected

STEP 1. For the past 12 hours, rate the **odor from hog operations** in the box for – *at home and outside, at home and inside, or not at home*. If you did not smell an odor, enter a **0** in the box that corresponds to your location(s) at that hour. If you were sleeping, enter a **Z**.

Use the scale to the right to rate the odor.

none	very faint…	faint…	moderate…	strong…	very strong			
0	1	2	3	4	5	6	7	8

Beginning last night:

	7 pm	8 pm	9 pm	10 pm	11 pm	12 am	1 am	2 am	3 am	4 am	5 am	6 am	7 am	8 am	9 am
Home-outside															
Home-inside															
Not home															

Reminder: Did you enter a number between 0 and 8 in at least one of the three boxes below each hour of the day?

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CHAPTER 3

MALODOR AS A TRIGGER OF STRESS AND NEGATIVE MOOD IN NEIGHBORS OF INDUSTRIAL HOG OPERATIONS

Introduction

Odor, noise, heat, and crowding are common environmental stressors [1]. Of interest here is the extensive literature on exposure to industrial odors and its effect on the physical and mental health of nearby residents. The sources of industrial odors vary and include solid and hazardous waste facilities, petroleum refineries, manufacturing facilities, and confined animal feeding operations (CAFOs). [1-37]

In the research on responses to odor as an environmental stressor, "annoyance" appears to be used more commonly than "stress". It is defined as a global marker of "discomfort summarizing different aspects… such as nuisance, disturbance, and unpleasantness" [38] and elsewhere as " 'a feeling of displeasure associated with any agent or condition believed to affect adversely an individual or a group' " [29]. It is consistently associated with odor perception and intensity in both laboratory and field studies [1, 3, 5, 19, 21, 28-30, 37-44].

Malodor and its effect on health and quality of life are concerns frequently expressed by neighbors of hog CAFOs [36]. Worry [19, 28], concern, and health-related concern [8, 14, 31] have been documented in neighbors of other industrial facilities. People living near

solid waste incinerators, landfills, and petroleum refineries, for example, voice many of the same issues expressed by neighbors of industrial hog operations: concerns about industrial emissions and odors, respiratory problems that they attributed to the emissions, perceived clusters of excess cancers, water pollution, property values, traffic, noise, pests; the inability to enjoy the outdoors or to hang clothes outside to dry; interrupted backyard barbecues and refinery deposits on cars and doorknobs. They express distrust of authorities who assured them that they did not need to worry about adverse health effects, a desire to be able to raise their children in a small town with fresh air, anger about being unfairly dumped on. CAFO neighbors and neighbors of other industrial facilities employ similar strategies to cope with unwelcome odors, including closing windows, keeping the house closed up, and staying indoors. [9, 14]

The Community Health Effects of Industrial Hog Operations (CHEIHO) study was a collaborative community based participatory research project, incorporating both quantitative and qualitative data collection. We collected air quality data in neighborhoods near hog CAFOs, collected health data from study participants, and conducted detailed ethnographic interviews of study participants; a full description of the methods can be found elsewhere [45]. In trying to understand documented health effects [4, 34, 36], we have hypothesized a stress-mediated effect of odor on health [2]; see, for example, Figure 1.1, which is adapted from the conceptual framework presented by Cohen, Kessler, and Gordon in Measuring Stress: A Guide for Health and Social Scientists [46]. Here we evaluate malodor as a potential environmental stressor and trigger of negative mood.

Methods

Data Collection

Persons eligible to participate in the CHEIHO study were non-smoking adults who lived within 1.5 miles of at least one hog CAFO and were willing to collect data twice daily for approximately two weeks. Data on the location of hog CAFOs relative to study participants and the average hog poundage per CAFO (known as steady state live weight, or SSLW) were obtained from the North Carolina Division of Water Quality. Participants attended a 3-hour training session where they learned to complete the required data collection activities. They selected a morning time and an evening time at which they would collect data (for example, 6:00 AM and 6:00 PM). Participants also completed the John Henryism Active Coping scale [47] and the Pearlin Mastery scale [48, 49] to assess coping and were tested for threshold odor sensitivity using butanol standards [50].

At the pre-selected, twice-daily times, participants spent 10 minutes outdoors at home and then returned indoors to rate any odor present during that 10 minute period on a 9-point scale where 0 = no odor and 8 = very strong odor. While outside, they also rated any odor they recalled for each hour in the previous 12 hours, by hour, whether at home outside, at home inside, or not at home. Following the odor rating, they responded to the following 5 questions: "How do you feel now… (a) Stressed or annoyed?, (b) Nervous or anxious?, (c) Gloomy, blue, or unhappy?, (d) Angry, grouchy, or bad-tempered, (e) Confused or unable to concentrate?" They rated how they felt on the same 9-point scale where 0 = not at all and 8 = extremely. The "Stressed or annoyed?" question was an ad hoc single-item measure [46, 51], and the remaining 4 questions came from the Profile of Mood States instrument, specifically, from the Tension-Anxiety, Depression-Dejection, Anger-Hostility, and

Confusion-Bewilderment subscales. (The Fatigue-Inertia and Vigor-Activity subscales were not used.)

Statistical Analyses

There were 2,058 records from 71 individuals in 16 communities. We performed a complete case analysis, restricting the data set to records for which the ratings of malodor, stress, and mood variables were non-missing. The final data set contained 1,883 records (91.5% of possible records).

Because data were repeated measures on individuals over time, we used mixed models in order to take into account the correlated structure of longitudinal data. For analyses of the effect of malodor on stress and mood, we used logistic mixed models. The stress and mood variables were re-coded as binary; for stressed or annoyed and nervous or anxious, 0 and 1 on the original scale were coded as 0 and 2-8 on the original scale were coded as 1. For the remaining 3 mood variables, 0 on the original scale was also coded as 0 and 1-8 on the original scale were coded as 1. The aforementioned coding decisions were made based on the distribution of the data such that approximately 90% of the records for each outcome variable were coded as 0 and approximately 10% were coded as 1.

We did not consider time-independent confounders because their relationship with exposure and outcome did not vary over time. We did, however, consider the following time-dependent covariates: time of day (morning vs evening), study day (1-14+), study week (first vs second), and whether or not participants reported a cold, flu, or stomach flu at any time during data collection (yes/no). We hypothesized that illness could affect both their ability to smell and/or perception of the odor and their mood.

A sample nonlinear mixed model follows:

Level 1 (Time, Within Person):

Logit ($Pr[Stress_{ij} = 1]$) = $\beta_{0j} + \beta_{1j}(odor)$;

where $Pr[Stress_{ij} = 1]$ is the probability that stress reported by person j at timepoint i equaled 1; β_{0j} is the person-specific intercept; and β_{1j} is the effect the time-dependent odor rating.

Level 2 (Between Person):

$\beta_{0j} = \gamma_{00} + \gamma_{01}(person_j) + \mu_{0j}$; $\mu_{0j} \sim N(0,\tau_{00})$

where β_{0j} is the person-specific intercept; γ_{00} is the mean of the person-specific intercepts (i.e., fixed intercept); $\gamma_{01}person_j$ is the contribution to the overall mean from person j; and μ_{0j} is the residual between-person variation in the intercept.

$B_{1j} = \gamma_{20} + \gamma_{21}(person_j) + \mu_{2j}$; $\mu_{2j} \sim N(0,\tau_{22})$

where β_{1j} is the person-specific effect of odor; γ_{20} is the mean of the person-specific effects (i.e., fixed effect); $\gamma_{21}person_j$ is the contribution to the overall odor effect from person j; and μ_{2j} is the residual between-person variation in the effect.

In addition to the logistic mixed models, we also ran linear mixed models for the analyses of the effect of odor on stress, treating odor as a linear term and the 9-level stress rating as a continuous variable [52] given its lower percentage of 0 ratings relative to the other 4 mood variables. We evaluated the following time-dependent potential confounders: time of day (morning vs evening), study day (1-14+), study week (first vs second), and whether or not participants reported a cold, flu, or stomach flu at any time during data collection (yes/no). We also evaluated the following potential modifiers of the effect of odor on stress: time of day (morning vs evening), gender (male vs female), age ($\leq$ 55.5 years vs > 55.5 years), mastery score (< 40 vs $\geq$ 40), John Henryism score (< 52 vs $\geq$ 52), and odor threshold ($\leq$ 40 vs > 40). We did not evaluate potential modifiers of the effect of odor on mood because there were very few nonzero reports of mood. Sample models follow.

Level 1 (Time, Within Person):

$$Stress_{ij} = \beta_{0j} + \beta_{1j}(odor) + r_{ij}; \qquad r_{ij} \sim N(0,\sigma^2)$$

where $Stress_{ij}$ is the stress level reported by person j at timepoint i; β_{0j} is the person-specific intercept; β_{1j} is the effect the time-dependent odor rating; and r_{ij} is the residual within-person variation.

When evaluating potential modification of the effect of reported odor on stress, the level 1 model was adjusted as follows:

$$Stress_{ij} = \beta_{0j} + \beta_{1j}(odor) + \beta_2(\text{effect modifier}) + \beta_{3j}(odor)(\text{effect modifier}) + r_{ij}; \quad r_{ij} \sim N(0,\sigma^2)$$

where $Stress_{ij}$ is the stress level reported by person j at timepoint i; β_{0j} is the person-specific intercept; β_{1j} is the effect of the time-dependent odor rating; β_2 is the effect of the time-independent effect modifier; β_{3j} is the interaction term; and r_{ij} is the residual within-person variation.

Level 2 models were the same as above.

For analyses of the effect of recalled hourly odor reported for each of the 12 hours preceding the reports of stress and mood, we considered time windows of varying widths: 1-hour, 2-hour, 3-hour, 4-hour, and 6-hour windows. For windows greater than 1 hour in width, we averaged the hourly odor ratings within the windows; all windows were mutually exclusive. We fit random intercepts only models for the lagged analyses; we did not include odor as a random effect because we lacked the sample size required to run models with ≤ 12 random effects for hourly odor. For example,

Level 1 (Time, Within Person):

$$Y_{ij} = \beta_{0j} + \beta_{1j}(odor_{t-1}) + \beta_{2j}(odor_{t-2}) + \ldots + \beta_{12j}(odor_{t-12}) + \beta_{13j}(\text{time of day}) + r_{ij}; \quad r_{ij} \sim N(0,\sigma^2)$$

where β_{1jk} is the effect of odor reported in the hour prior to data collection, β_{2jk} is the effect of odor reported 2 hours prior, … β_{12jk} is the effect of odor reported 12 hours prior, β_{13jk} is the effect of time of day (morning or evening), and r_{ijk} is the residual within person variation.

Results

Descriptive analyses

Table 3.1 presents demographic information about study participants. The median age was 55.5 years and ranged from 19.2 years to 84.6 years. Approximately two-thirds of the participants were female, and approximately 80% were black. 77% of participants reported that they grew up around livestock. Of the 16 communities in which participants lived, 6 communities were within 2 miles of 1-4 CAFOs, 4 were within 2 miles of 5-9 CAFOs, and 6 communities were within 2 miles of 10 or more CAFOs. The average SSLW within 2 miles of participants' communities ranged from 0.6 to 11 million pounds.

The distributions of the independent variables are presented in Table 3.2. Of the 1,883 odor ratings recorded after participants spent 10 minutes outdoors, 42% equaled zero. An additional 30% were low on the 9-point scale. Approximately 1% of the data were in each of the two highest categories. A much larger percentage of non-missing hourly odor ratings equaled zero, which reflects the fact that participants spent more time inside their homes or away from home where hog odor was less frequently present. (Recall that participants rated hourly hog odor whether at home outdoors, at home indoors, or away from home.) Approximately one-third of hourly odor ratings were missing, defined as the proportion of the total number of hours of participation for which participants failed to rate odors or note that they were asleep.

Most of the ratings of stress and mood equaled zero. For "Stressed or annoyed?", 75% of reports were zero; 82% were zero for "Nervous or anxious?", 85% for "Gloomy, blue, or unhappy?", 91% for "Angry, grouchy, or bad-tempered?", and 93% for "Confused or

unable to concentrate?". There were very few ratings at the high end of the scale for the first 4 variables in the above list and no high ratings for the last of the above (Table 3.3).

Mixed models

Though participants were recruited in neighborhoods, we did not include a 3rd level, a neighborhood level, in the mixed models. 3-level models did not converge; there did not appear to be any remaining variation between neighborhoods once the variations within and between people were in the models. We modeled the intercept as a random term in order to capture the variation between participants in baseline (average) levels of stress and mood. We also modeled the odor rating following 10 minutes outdoors as a random effect; variance estimates for the odor effect were large relative to their standard errors, and Akaike Information Criterion (AIC) values decreased markedly when odor was included as a random, as opposed to fixed, term. We evaluated the odor rating as a nominal variable using indicator terms (Figure 3.2); we found an approximately linear relationship between odor and stress and included odor as a single linear term in final models. Associations between odor and mood variables were similarly linear, though not as steep in slope. None of the time-dependent confounders we considered changed the magnitude of the beta coefficients for odor.

Table 3.4 presents odds ratios and confidence intervals for analyses of the effect of odor rated twice daily after 10 minutes outdoors on the binary (yes/no) stress and mood variables. The ratio of the odds of reporting stress for a 1-unit increase in reported odor was 1.7 (95% CI: 1.42 – 2.08). Consequently, a 4-unit change on the odor scale (from odor = 0 to odor = 4, for example) yields an odds ratio of 8.7. Odds ratios for feeling nervous, gloomy,

angry, and unable to concentrate, associated with a 1-unit change in odor, were 1.67 (95% CI: 1.25 – 2.22), 1.58 (95% CI: 1.06 – 2.36), 1.38 (95% CI: 1.10 – 1.73), and 1.50 (95% CI: 1.03 – 2.18), respectively.

Table 3.5 presents the beta coefficients for the effect of odor rated after 10 minutes outdoors on reported stress, stratified by potential modifiers. The effect of time of day is moderate, with a lower beta coefficient for the effect of odor in the evening than in the morning. Age and John Henryism score were stronger modifiers. Older people had beta coefficients approximately twice the magnitude of younger people, and the effect of odor in people who scored high on the John Henryism scale is almost 3 times that in people with lower scores. Gender, mastery score, or odor threshold did not modify the association between odor and stress.

Analyses of the effect of hourly odor in various time windows (recalled odor reported for the 12 hours prior to twice daily data collection) produced no discernible pattern. Estimated beta coefficients were generally smaller than the beta coefficient estimated for odor reported after 10 minutes outdoors and shortly before rating of stress/mood (no lag). Furthermore, the coefficients varied in magnitude and in sign (both positive and negative), neither increasing nor decreasing consistently with temporal distance from the assessment of stress/mood. Because the hourly odor data were recalled up to 12 hours prior to the time at which the data were reported, measurement error may partially explain the inconsistent results.

Discussion

Our aim here was to evaluate the effect of malodor from industrial hog farms on stress and mood reported by neighboring residents. We found that ratings of feeling stressed/annoyed, nervous/anxious, gloomy/unhappy, angry/grouchy, and confused/unable to concentrate increased with ratings of malodor reported after participants spent 10 minutes outdoors. Of the 5 outcome variables, odor was most strongly related to stress/annoyance. Age and John Henryism score appeared to be modifiers of that relationship, with older people and those with higher John Henryism scores more affected by malodor. Time of day was a potential modifier, with the odor effect somewhat diminished in the evenings compared to mornings.

There is a consistent literature documenting the effect of malodor on annoyance, both in the laboratory [1, 37, 38, 43, 44] and in the "real world" [3, 29, 30]. Several authors have also considered age and/or coping style as potential effect modifiers [1, 3, 29, 30, 37]. In the German studies of annoyance response to industrial odors, people with higher scores for problem-oriented coping, or action-oriented coping, tend to report more annoyance following odor exposure than do people with lower scores [3, 29, 30, 37]. Asmus and Bell, however, did not find coping style to be an effect modifier in their U.S. laboratory study, though because the results were not significant, they were not reported [1]. It is possible that the findings on coping differ because the studies used different instruments to assess coping and/or because the German studies took place in the field, while the U.S. study took place in the laboratory.

Our results on modification by coping status, a stronger relationship between odor and stress in participants with high John Henryism scores, are consistent with the studies by Steinheider [29], Winneke [37], Sucker [30], and Both [3]. They are also consistent with our

hypothesis that those who perceive that they have more control, when faced with an unpredictable and uncontrollable stressor, would find malodor more stressful than those who perceive they have less control. Work by Dressler et al [53] and Williams and Lawler [54] suggested an interaction between John Henryism and gender in the relationship between John Henryism and illness. Dressler et al found a positive relationship between John Henryism score and both blood pressure and hypertension in men but a negative relationship in women [53]. Williams and Lawler, in a convenience sample of low-income women, did not observe a relationship between John Henryism and 12-month illness, as measured by the Seriousness of Illness Rating Scale [54]. We did not further stratify by gender our subgroups defined by John Henryism score, given concern about the sample size required to include a 3-way interaction term in the preceding statistical models, but future work should consider a potential John Henryism by gender interaction.

Steinheider [29], Winneke [37], Sucker [30], and Both [3] also considered age as an effect modifier and have observed that older people are less annoyed by odors than are younger people, an effect they attribute to “so-called old-age bias: the age-related increase of generalized satisfaction with a wide spectrum of environmental conditions". We observed the opposite effect for age as a modifier. It is possible that we observed a greater effect of odor on stress in older people because they are retired and tend to be home more often. However, this hypothesis explains the conflicting results only if the activity patterns of older adults differed between this study and other the study populations.

We hypothesized that modification by time of day, if any, would point to a stronger relationship between odor and stress in the evenings, after participants had experienced the hassles of the day, though that is not what we observed. Nonetheless, the magnitude of the

potential modification by time of day was small, compared to that by age and John Henryism score. We are not aware of other work that has considered the effect of time of day; neither are we aware of another study that is longitudinal in nature.

The longitudinal design was a particular strength of this research. There were approximately 28 repeated measures for each participant. In the analyses, each participant served as his/her own control; thus, for example, his/her rating of stress when odor was present was compared to his/her rating of stress when it was absent. Perception of odor and perception of stress and adverse mood vary between people, and we were able to statistically model the between-person variation in the effect of odor on stress/mood.

Our results on the effect of reported odor on mood are consistent with the results that Schiffman et al observed [26]. They evaluated effects of hog odor on mood; neighbors completed Profile of Mood States (POMS) questionnaires on each of 4 days when odors were present, while matched controls completed the questionnaire on each of 2 days. POMS scores were higher in neighbors, who reported more tension, depression, anger, fatigue, confusion, and less vigor. We were able to improve on their study design in two respects. First, participants selected times for twice daily data collection prior to beginning their study participation. They did not choose times of day to collect data based on whether the odor was present or not; i.e., exposure status did not influence the selection of data collection times. Second, as mentioned above, participants served as their own controls; thus mood ratings provided by an exposed group did not have to be compared to ratings provided by another unexposed group.

Our assessment of stress and mood was limited in that we did not ask participants to identify the source of the stress and/or negative mood. After spending 10 minutes outdoors,

they were asked to rate any odor present and then to respond to the question, "How do you feel now?... Stressed or annoyed? Nervous or anxious?" et cetera. We could observe a spurious association between odor and stress, for example, if a stressor that is unrelated to odor occurs when odor is present. Given the longitudinal design, however, the coincidence of odor and an unrelated stressor would need to be repeated over time in order to produce a spurious association.

A further design limitation was the contemporaneous assessment of both exposure and outcome. Because both exposure and outcome were assessed contemporaneously, by self-report, it is difficult to determine how the assessment of one affected the assessment of the other. Participants spent 10 minutes outdoors before returning indoors to complete the required data collection activities; they rated the intensity of any malodor present and then rated any stress and/or adverse mood. If an odor were present, and if it had an effect on the participant's stress/mood, s/he rated both odor and stress/mood while experiencing that stress, annoyance, and negative mood. Rating the odor while stressed or annoyed, for example, may have induced a higher rating than the participant would have rated in the absence of feeling stressed or annoyed.

In a community based, longitudinal study of the health effects of residential exposure to emissions from industrial hog operations, we have observed a negative effect of malodor on stress and mood. Our findings are consistent with a large literature on malodor as an environmental stressor. We observed the largest effect for odor on stress and/or annoyance;

annoyance is the predominantly assessed outcome in the literature, defined as “discomfort summarizing different aspects… such as nuisance, disturbance, and unpleasantness” [38] or “ ‘a feeling of displeasure associated with any agent or condition believed to affect adversely an individual or a group’ ” [29]. We conclude that malodor does appear to have such an effect on nearby residents unwillingly exposed at home.

Table 3.1. Characteristics of Participants in the CHEIHO study.

	n records	N participants
Age		
> 55.5 years	991	36
≤ 55.5 years	892	35
Gender		
Female	1272	49
Male	611	22
Race		
Black	1511	59
Not black[a]	372	12
Grew up around livestock		
Yes	1443	55
No	363	13
Missing	77	3
Total	*1883*	*71*

[a] 11 white participants and 1 Latino participant

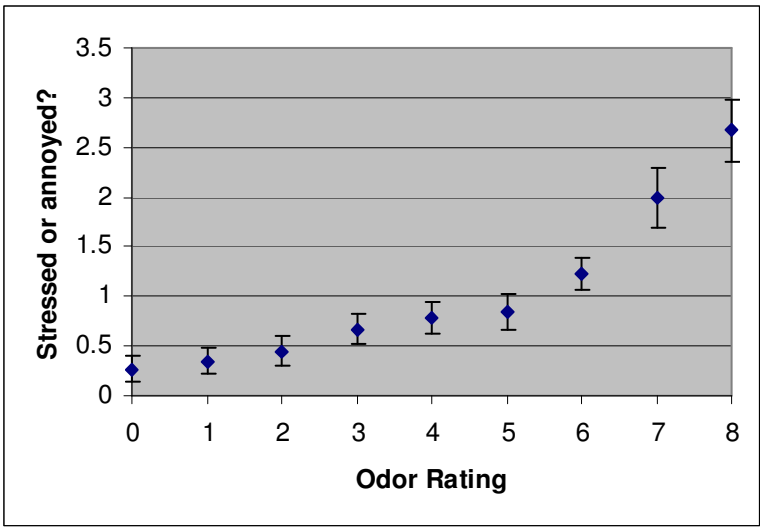
Table 2. Number (%) of Records, n, and Number of Participants, N, in Each Category of the Independent Variables.

	Odor Rating After 10 Minutes Outdoors			Hourly Odor Ratings		
Level	**n**	**%**	**N**	**n**	**%**	**N**
0	791	42.0	60	14194	81.9	71
1	351	18.6	59	902	5.2	62
2	220	11.7	56	666	3.8	58
3	179	9.5	57	456	2.6	53
4	120	6.4	45	363	2.1	53
5	70	3.7	39	218	1.3	48
6	106	5.6	39	269	1.6	44
7	22	1.2	11	122	0.7	30
8	240	1.3	12	136	0.8	29
Total	*1883*	*100.0*	*71*	*17326*	*100.0*	*71*

Table 3.3. Number (%) of Records, n, and Number of Participants, N, in Each Category of the Dependent Variables.

	Stressed or Annoyed?			Nervous or Anxious?			Gloomy, Blue, or Unhappy?			Angry, Grouchy or Bad-tempered?			Confused or Unable to Concentrate?		
Level	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**	**N**
0	1416	75.2	68	1551	82.4	70	1597	84.8	69	1720	91.3	70	1752	93.0	70
1	263	14.0	51	203	10.8	34	168	8.9	36	95	5.1	33	93	4.9	22
2	89	4.7	37	77	4.1	22	35	1.9	14	19	1.0	9	18	1.0	7
3	50	2.7	22	34	1.8	12	43	2.3	14	9	0.5	7	10	0.5	5
4	14	0.7	10	10	0.5	2	12	0.6	6	5	0.3	4	7	0.4	3
5	18	1.0	12	5	0.3	5	9	0.5	5	13	0.7	8	2	0.1	2
6	19	1.0	10	1	0.1	1	8	0.4	5	10	0.5	4	1	0.1	1
7	6	0.3	4	1	0.1	1	6	0.3	3	4	0.2	2	0	0.0	0
8	8	0.4	5	1	0.1	1	5	0.3	3	8	0.4	3	0	0.0	0
Total	*1883*	*100.0*	*71*	*1883*	*100.0*	*71*	*1883*	*100.0*	*71*	*1883*	*100.0*	*71*	*1883*	*100.0*	*71*

Figure 3.1. Beta Coefficients, with Standard Errors, from Linear Mixed Models of the Effect of Odor Reported after 10 Minutes Outdoors on Stress[a]



[a] With the intercept and odor included as random effects, and odor coded as a series of indicator variables.

Table 3.4. Ratios of the Odds of Reporting Stress/Mood for a Single Unit Increase in Odor Reported after 10 Minutes Outdoors, from Nonlinear Mixed Models with Stress/Mood as Binary Variables[a]

	Odds Ratio	95% CI
Stressed or annoyed?	1.72	1.42 – 2.08
Nervous or anxious?	1.67	1.25 – 2.22
Gloomy, blue, or unhappy?	1.58	1.06 – 2.36
Angry, grouchy, or bad-tempered?	1.38	1.10 – 1.73
Confused or unable to concentrate?	1.50	1.03 – 2.18

[a] With the intercept and odor rating (0-8) included as random effects

Table 3.5. Associations Between Odor Reported after 10 Minutes Outdoors and Stress from Linear Mixed Models, Stratified by Modifiers[a]

	β	SE	95% CI
Odor rating			
All records	0.16	0.03	0.10 – 0.22
Morning	0.19	0.03	0.12 – 0.25
Evening	0.14	0.03	0.07 – 0.20
Age ≤ 55.5 years	0.11	0.05	0.02 – 0.20
Age > 55.5 years	0.21	0.04	0.12 – 0.29
Low John Henryism	0.08	0.05	-0.01 – 0.18
High John Henryism	0.22	0.04	0.14 – 0.30

[a] With the intercept and odor rating (0-8) included as random effects

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CHAPTER 4

THE EFFECT OF REPORTED MALODOR, STRESS, AND NEGATIVE MOOD ON SECRETORY IMMUNE FUNCTION IN NEIGHBORS OF INDUSTRIAL HOG OPERATIONS

Introduction

In North Carolina, the average hog inventory on any given day is approximately 10 million hogs [1]. Recent data indicate that 97% of hogs were raised in facilities of at least 2000 animals [2]. These confined animal feeding operations (CAFOs) release complex mixtures of dusts and gases from confinement houses (large buildings where animals are housed), waste lagoons (open-air pits where waste is stored), and spray fields (adjacent fields where waste is sprayed as fertilizer). Airborne emissions include organic dusts, endotoxins, ammonia, hydrogen sulfide, and volatile organic compounds, many of which are odorants.[3]

Odor and its effects on health and quality of life are primary concerns for neighbors of hog CAFOs. Neighbors describe odors as highly noxious; odors are unpredictable and uncontrollable. Malodors curtail their ability to enjoy their homes and to spend time outdoors [4]. Exposure is not equitable. People of color and poor people are more likely to live near hog CAFOs than are people who are white and/or wealthy [5]; likewise, students of color and poor students in North Carolina are more likely to attend (middle) schools near hog CAFOs [6].

The health effects of occupational exposure to dusts, gases, and pathogens inside hog confinement houses have been examined extensively (for example, [7-22]); effects of exposure among neighbors, however, have been examined less extensively. A small number of studies of neighbors have suggested adverse effects such as negative mood [23], more frequent headache, diarrhea, burning eyes, runny nose, sore throat, cough [4] and other respiratory effects [24], decreased immune function [25], more frequent asthma symptoms [26, 27], and decreased lung function [27]. Relative to occupational exposures, health effects in neighbors are reported at lower levels of exposure [28].

Potential explanations include both toxicologic and non-toxicologic mechanisms [28]. Here we examine the non-toxicologic hypothesis that exposure to unpredictable and uncontrollable odors from hog CAFOs has a psychophysiologically mediated effect on health, specifically, that odor as a stressor has an immunosuppressive effect on secretory immunoglobulin A (sIgA) (Figure 1.1). sIgA functions as a first line of defense against pathogens entering the body via the mucosal epithelia of the gastrointestinal, respiratory, and genitourinary tracts [29, 30]. Like other immune markers, it is responsive to stressors, though the direction of the response appears to depend on the type and duration of the stressor [31-35].

We assessed perceptions of odor, stress/annoyance, anxiety, unhappiness, anger, and confusion and measured salivary sIgA secretion rates in the Community Health Effects of Industrial Hog Operations (CHEIHO) study. CHEIHO was a quantitative and qualitative study of the effects of hog CAFOs on the health and quality of life of eastern North Carolina residents. The aim of the present study was to evaluate potential associations between perceived odor, stress, mood, and secretory immune function.

Materials and Methods

Persons eligible to participate in the CHEIHO study were non-smoking adults who lived within 1.5 miles of at least one hog CAFO in eastern North Carolina. Data on the location of hog CAFOs relative to study participants and the steady state live weight (SSLW), average hog poundage per CAFO, were obtained from the North Carolina Division of Water Quality. If eligible, multiple adults per household were permitted to participate. One hundred and two participants from 16 neighborhoods collected data twice daily for approximately two weeks; they were permitted to participate for an additional week if odor frequency was low during the initial two weeks. The CHEIHO study was designed to address multiple hypotheses, one of which we address here. A full description of the study methods, including the monitoring of air pollutants from hog CAFOs, can be found elsewhere [36].

Study participants attended a 3-hour training session on the evening preceding the commencement of data collection; there they learned to complete the required data collection activities. Participants selected the times at which they would collect data (for example, 7:00 AM and 7:00 PM), at least one hour after eating, drinking, or brushing teeth. They collected data independently in their own homes. Project staff were available by phone and visited participants in person at the end of the first week to review progress, answer questions, and correct problems.

Independent variables

Twice daily, participants spent 10 minutes outside. While outside, they recorded hourly ratings of recalled odor from hog CAFOs for the preceding 12 hours, whether at home outside, at home inside, or away from home, on a 9-point scale where 0 = no odor and 8 = very strong odor. Following the prescribed 10-minute exposure, they returned indoors and rated the odor for that 10-minute period on the same 9-point scale. Participants then responded to the following 5 mood questions, on a 9-point scale where 0 = not at all and 8 = extremely, "How do you feel now… Stressed or annoyed? Nervous or anxious? Gloomy, blue, or unhappy? Angry, grouchy, or bad-tempered? Confused or unable to concentrate?"

The "Stressed or annoyed" question was an ad-hoc single item measure designed to assess primary appraisal of malodor exposure as potentially stressful (see Figure 4.1) [37, 38]. The other four questions were from four of the six sub-scales of the Profile of Mood States instrument [23, 39], reflecting the Tension-Anxiety, Depression-Dejection, Anger-Hostility, and Confusion-Bewilderment mood states; questions from the Fatigue-Inertia and Vigor-Activity sub-scales were not used.

Initial analyses of sIgA and odor reported twice daily after 10 minutes outdoors, where the 9-level odor rating was included as a series of 8 indicator variables, suggested a nonlinear relationship. We therefore re-coded this odor variable as a threshold linear term [25] (Table 4.1). Similar analyses of sIgA and the stress/mood variables, where each variable was included as a series of 8 indicator variables, also suggested nonlinear relationships. In particular, the relationships between sIgA and "stressed or annoyed", "angry, grouchy, or bad-tempered", and "gloomy, blue, or unhappy" suggested a binary coding; we therefore re-coded all of the stress and mood variables (for consistency) as binary variables (Table 4.1).

Covariates

We evaluated the following time-dependent covariates as potential confounders: time of day at which the saliva sample was collected, study day, study week, weekday versus weekend, and whether or not the participant reported suffering a cold, flu, or stomach flu at the time s/he collected data (Table 4.1). We considered time of day because previous work suggested that average odor was higher and average sIgA levels were lower in the evening than in the morning [25]. Study day/week were considered as potential markers of a training effect. We hypothesized that illness might confound because of its ability to affect sense of smell and immune function. We considered one time-dependent potential modifier of the relationship between odor and sIgA: whether or not the participant reported irritation of the eyes, nose, throat, skin, or cough after the prescribed 10-minute outdoor exposure. We hypothesized that symptoms of irritation could suggest exposure to co-constituents of the odor plume that might trigger an inflammatory immune response [8, 9, 11, 12, 40-43].

We did not consider time-independent factors, such as age or gender, to be confounders because their association with exposure and outcome did not vary over the 2+ week period of data collection. We did, however, consider time-independent factors as potential effect modifiers of the relationship between sIgA secretion and both reported odor and stress (Table 4.1). Study participants completed the John Henryism Active Coping scale [44] and the Pearlin mastery scale [45, 46]; we considered John Henryism and mastery as potential effect modifiers hypothesizing that participants engaged in high effort coping were more likely to be physiologically responsive to stressors. Participants were also tested to

determine their threshold sensitivity to odor using butanol standards [47] to evaluate whether participants with a better sense of smell were more responsive to the effects of odor.

Dependent variable

Study participants collected 2-minute unstimulated whole saliva samples in pre-weighed collection tubes. They stored samples in their home freezer for the duration of their participation. Project staff transferred samples back to UNC on dry ice, where samples were stored at -20 ^{o}C until they were post-weighed. Samples were then stored at -80 ^{o}C until they were shipped by overnight mail on dry ice to Salimetrics, LLC for sIgA analysis. We did not send all samples for analysis, but rather selected all samples from any participant who rated at least one 10-minute odor episode greater than 3 on the 9-point scale during their 2+ weeks of study participation (2150 samples from 73 participants).

Samples were assayed in duplicate for salivary secretory IgA by Salimetrics, LLC (State College, PA) using an enzyme immunoassay. The test used 25 µl of saliva, had a lower limit of detection of 2.5 µg/mL, standard curve range from 2.5 µg/mL to 600 µg/mL, and average intra-and inter-assay coefficients of variation of 5.6% and 8.8%, respectively. Samples greater than 600 µg/mL were diluted until they were within range. The correlation between the duplicates was high (r = 0.98). The average of the duplicates was used as the outcome in statistical analyses.

Statistical analysis

We used a mixed model to assess the relationships between sIgA secretion and both odor and stress/mood. The model accounted for the correlated structure of longitudinal data (SAS statistical software version 9.1, SAS Institute, Inc., Cary, NC). The model had two levels – within person (between time points) and between person. A sample model follows:

Level 1 (Time, Within Person):

$$\ln(\text{sIgA secretion rate})_{ij} = \beta_{0j} + \beta_{1j}(\text{exposure}) + \beta_{2j}(\text{time of day}) + r_{ij}; \qquad r_{ij} \sim N(0,\sigma^2)$$

where $\ln(\text{sIgA secretion rate})_{ij}$ is the natural log of the sIgA secretion rate (μg/min) for person j at timepoint i; β_{0j} is the person-specific intercept; β_{1j} is the effect of the time-dependent exposure of interest; β_{2j} is the effect of time of day; and r_{ij} is the residual within-person variation.

When evaluating potential modification of the effect of exposure on sIgA secretion rate, the level 1 model was adjusted accordingly:

$$\ln(\text{sIgA secretion rate})_{ij} = \beta_{0j} + \beta_{1j}(\text{exposure}) + \beta_{2j}(\text{time of day}) + \beta_3(\text{effect modifier}) + \beta_{4j}(\text{exposure})(\text{effect modifier}) + r_{ij}; \qquad r_{ij} \sim N(0,\sigma^2)$$

where $\ln(\text{sIgA secretion rate})_{ij}$ is the natural log of the sIgA secretion rate (μg/min) for person j at timepoint i; β_{0j} is the person-specific intercept; β_{1j} is the effect of the time-dependent exposure of interest; β_{2j} is the effect of time of day; β_3 is the effect of the time-

independent effect modifier; β_{4j} is the interaction term; and r_{ij} is the residual within-person variation.

Level 2 (Between Person):

$$\beta_{0j} = \gamma_{00} + \gamma_{01}(person_j) + \mu_{0j}; \qquad \mu_{0j} \sim N(0,\tau_{00})$$

where β_{0j} is the person-specific intercept; γ_{00} is the mean of the person-specific intercepts (i.e., fixed intercept); $\gamma_{01}person_j$ is the contribution to the overall mean from person j; and μ_{0j} is the residual between-person variation in the intercept.

$$\beta_{2j} = \gamma_{20} + \gamma_{21}(person_j) + \mu_{2j}; \qquad \mu_{2j} \sim N(0,\tau_{22})$$

where β_{2j} is the person-specific effect for time of day; γ_{20} is the mean of the person-specific effects (i.e., fixed effect); $\gamma_{21}person_j$ is the contribution to the overall time of day effect from person j; and μ_{2j} is the residual between-person variation in the effect.

Lagged Analyses

Because we collected data on recalled exposure to odor from hog CAFOs in the hours preceding the completion of the morning and evening data collection protocol, we were able to evaluate the relationship between recalled odor at various lags and sIgA secretion rate. We calculated average and peak hourly odor ratings for 1-, 2-, 3-, 4-, and 6-hour time windows, up to 12 hours prior to time at which each saliva sample was collected. Time windows were mutually exclusive and were included as multiple independent variables in the

same model. In evaluating relationships between sIgA secretion and the stress/mood variables, not only did we consider stress and mood reported shortly (minutes) before saliva sample collection, but we also considered the effect of stress and mood reported approximately 12 and 24 hours prior.

Influence Diagnostics

To examine potentially influential data points and/or people, we used the influence option available in SAS 9.1 We evaluated overall influence via the restricted likelihood distance, influence over the magnitude of the beta coefficients using the D and MDFFITS statistics, and influence over the precision of the betas using the covariance trace and covariance ratio statistics. [48]

Consent and Confidentiality

The CHEIHO study was approved annually by the Institutional Review Board of the University of North Carolina at Chapel Hill, and all study participants consented to participate. In addition to the standard activities employed to maintain confidentiality of study participants, we obtained a Certificate of Confidentiality from the U.S. Department of Health and Human Services. The certificate protects identifying information even under court order or subpoena, which is important given the political nature of research in the health effects of hog CAFOs in the state of North Carolina. Institutional Review Board approval was also obtained for the analyses conducted in Chapters 3 and 4.

Results

Descriptive analyses

After exclusions, we analyzed 1,957 records from 71 participants in 16 communities (Figure 4.2). The number of days of participation per person ranged from 11 to 22, and 70% of participants collected data for exactly 14 days. Participant ages ranged from 19 to 85 years, with a median age of 56 years. 49 (70%) participants were female, 59 (83%) were black, and 55 (77%) grew up around livestock. (Table 4.2) Of the 16 communities in which participants lived, 6 communities were within 2 miles of 1-4 CAFOs, 4 were within 2 miles of 5-9 CAFOs, and 6 communities were within 2 miles of 10 or more CAFOs. The average SSLW within 2 miles of participants' communities ranged from 0.6 to 11 million pounds.

Study participants provided 1,957 saliva samples that were analyzed for sIgA content; sIgA secretion rates were log normally distributed and strongly skewed to the right (Figure 4.3). The average secretion rate was 135.1 μg/min, and the median was 88.3 μg/min. The standard deviation was 194.0 μg/min, and the secretion rates ranged from 1.9 μg/min to 2,791.7 μg/min.

For the 1,957 records with complete secretion rate data, there were 1,846 odor ratings following the 10-minute prescribed outdoor exposure (6% missing); 1,917 responses to the question, "Stressed or annoyed?" (2% missing); 1,912 responses to "Nervous or anxious?" (2% missing); 1,912 responses to "Gloomy, blue, or unhappy?" (2% missing); 1,913 responses to "Angry, grouchy, or bad-tempered?" (2% missing); and 1,907 responses to "Confused or unable to concentrate?" (3% missing). Odor ratings were zero for 39% of the time, low (rating = 1,2) 29% of the time, moderate (rating = 3-5) 19% of the time, and high (rating = 6-8) 8% of the time. Stressed ratings were zero for 72% of the time and high for

only 2% of the time. Nervous ratings were zero approximately 80% of the time and high for only 0.3% of the time. Gloomy ratings were zero for 82% of the time and high only 1% of the time. Ratings of anger and confusion/poor concentration were even less frequent, equal to 0 for 88% and 90% of the time, respectively. Confusion/poor concentration was never reported at the two highest levels. (Table 4.3)

Model analyses

Though participants were recruited in communities, we did not include the community level in the mixed models because the community-level variation in sIgA secretion rates was negligible with person-level variation in the model. Exposure variables were modeled as fixed effects. We modeled the intercept as random in order to permit average sIgA levels to vary between people, and we included time of day as a random effect because its effect on sIgA secretion varied between people. None of the other time-dependent covariates functioned as confounders. We did not consider effect modification of the relationships between adverse mood and sIgA because there were relatively few reports of nonzero adverse mood (Table 4.3).

Relationships between sIgA secretion rate and odor reported twice daily after 10 minutes outdoors, stratified by modifiers of interest, are presented in Table 4.4. There does not appear to be an overall effect of malodor on sIgA secretion rate, nor does there appear to be modification by time of day, age, gender, mastery score, or whether or not the participant reported irritation of the eyes, nose, throat, skin, or cough. There appears to be potential modification by John Henryism score and by the score on the butanol threshold test for odor

sensitivity. Beta coefficients are positive at low John Henryism and high butanol scores; they are negative at high John Henryism and low butanol scores.

Table 4.5 presents data on associations between sIgA secretion rate, stress, and mood. The data do not suggest an overall effect for feeling stressed, nervous, gloomy, confused or unable to concentrate. There does appear to be a negative effect of feeling angry, grouchy, or bad-tempered on sIgA secretion. With respect to modification of the relationship between sIgA secretion and reported stress, there is potential modification by time of day; the effect appears to be present in the evening, as opposed to the morning. The effect is strongly negative among older participants, with no effect in younger participants. Participants with lower scores on the mastery and John Henryism scales display more strongly negative effects of reported stress on sIgA. Gender was not a modifier.

Examination of influence statistics revealed one particularly influential person, according to multiple markers of influence (overall influence, influence over beta coefficients, covariance parameters, etc.). Exclusion of the influential participant tended to decrease the magnitude of the beta coefficient in the subgroups where she was included. For example, the beta coefficients for high John Henryism score and low butanol score in Table 4.4 decrease from -0.12 to -0.07 and from -0.10 to -0.06, respectively, when she was excluded. Of note in Table 4.5 are the changes in the beta coefficients for the older age group, for feeling angry, grouchy, or bad-tempered, and for feeling nervous or anxious; these beta coefficients changed from -0.29 to -0.12, -0.25 to -0.06, and -0.23 to -0.38, respectively.

Analyses of hourly odor ratings lagged up to 12 hours prior to saliva sample collection, in time windows of varying widths, were conducted. Neither variable coding, window width, nor number of hours prior to sample collection affected the result; beta

coefficients varied in magnitude and in direction, with no discernible pattern or trend. Because the hourly odor data were recalled up to 12 hours prior to the time at which the data were reported, measurement error may partially explain the inconsistent results. With respect to stress/mood ratings lagged approximately 12 and 24 hours prior to saliva sample collection, beta coefficients tended to be strongest for the concurrent (Table 4.5), as opposed to lagged, ratings, with the exception of reported confusion/poor concentration for which there was no association at all.

Discussion

We found little evidence of an association between sIgA secretion rate and malodor from hog CAFOs. There was a suggestion of an effect at the highest levels of odor reported after 10 minutes outdoors and confined to particular subgroups of the study population. The observed effect of reported stress on sIgA secretion, if any, was also confined to particular subgroups. Of the four mood variables we evaluated, feeling angry, grouchy, or bad-tempered appeared to have an effect on sIgA secretion, but that was attributable to a single participant. Feeling nervous or anxious did not have an effect in the full study population but did appear to have an effect if that participant was excluded. The influential person affected the results in part because her secretion rates varied over a wide range, from 12 µg/min to 2,800 µg/min; she contributed the highest secretion rates to the data set. She also contributed 20% of the highest odor ratings (odor = 8), 16% of the higher stress ratings (stressed = 5-8), 12.5% of the higher nervous ratings, 14% of the higher gloomy ratings, and 25% of the higher angry ratings. Her highest sIgA secretion rates were at times when she reported low

to moderate odor levels; her strongly negative slope (β=-0.17) consequently affected the average slope for the full study population.

There was a suggestion of an association between malodor and sIgA in several subgroups stratified by John Henryism score and by butanol score. The beta coefficients for low John Henryism and high butanol were positive, while the coefficients for high John Henryism and low butanol were negative. While we expected a negative effect of odor on sIgA, or no effect, we did not necessarily expect to observe a positive effect of odor on sIgA secretion. The literature on stress and sIgA secretion includes both positive and negative effects; acute and active coping stressors tend to be associated with positive effects, while chronic and passive coping stressors tend to be associated with negative effects [31-34]. Malodor is a chronic stressor that occurs in acute episodes, which we considered a passive coping stressor because it is unpredictable and uncontrollable – hence the expected negative effect. It is certainly possible, however, that subgroups of exposed residents perceive the odor differently. Furthermore, it is possible that some are not responding to odor as a stressor, but are instead responding to bioaerosol constituents of the odor plume that are immunostimulatory.

Stress was negatively associated with sIgA among older people and those with low John Henryism scores; there appeared to be no association between stress and sIgA among younger people and those with high John Henryism scores. Older people may be more susceptible to an odor-induced effect of stress on sIgA secretion because they tend to spend more time at home, if retired. Given Sherman James's original work on John Henryism [44], we might expect a negative association for those with high, as opposed to low, John Henryism scores, reasoning that people who sense that they should have control would be

more adversely affected when exposed to an uncontrollable stressor. However, the work by James et al was conducted in a study population of men; more recent work has suggested an interaction between John Henryism and gender in the association between John Henryism and illness. Dressler et al [49] found a positive relationship between John Henryism and blood pressure and hypertension in men but a negative relationship in women, and Williams and Lawler [50] found no relationship between John Henryism scores and illness, as measured by the Seriousness of Illness Rating Scale in a study population of low income women. We did not investigate the interaction between John Henryism and gender because we lacked an adequate sample size for a 3-way interaction term ([odor × John Henryism × gender] or [stress × John Henryism × gender]), but future work should attempt to do so.

John Henryism scores modified relationships between malodor and sIgA and stress and sIgA differently. When reporting stress, participants did not indicate the source of the stress; after spending 10 minutes outside, they rated any odor present and then rated their stress level. When exposed to malodor, participants could report stress prompted by that exposure; they could also report stress unrelated to odor that nonetheless occurred concurrently. Both would tend to make odor-sIgA and stress-sIgA results converge. However, stress reported at times when malodor was absent would lead odor-sIgA and stress-sIgA results to diverge and may partially explain the differences in the role of John Henryism as a modifier. The distribution of men and women in the subgroups defined by John Henryism score and the modification by gender of the odor-sIgA association but not the stress-sIgA association may also explain the differences observed here.

Above we have interpreted the observed subgroup effects of malodor and stress on sIgA. However, the apparent effect modification may be a function of other factors,

including unmeasured time-dependent confounders, unmeasured time-independent modifiers, and/or measurement error. Overall we found little evidence of an effect of either malodor or stress on sIgA secretion.

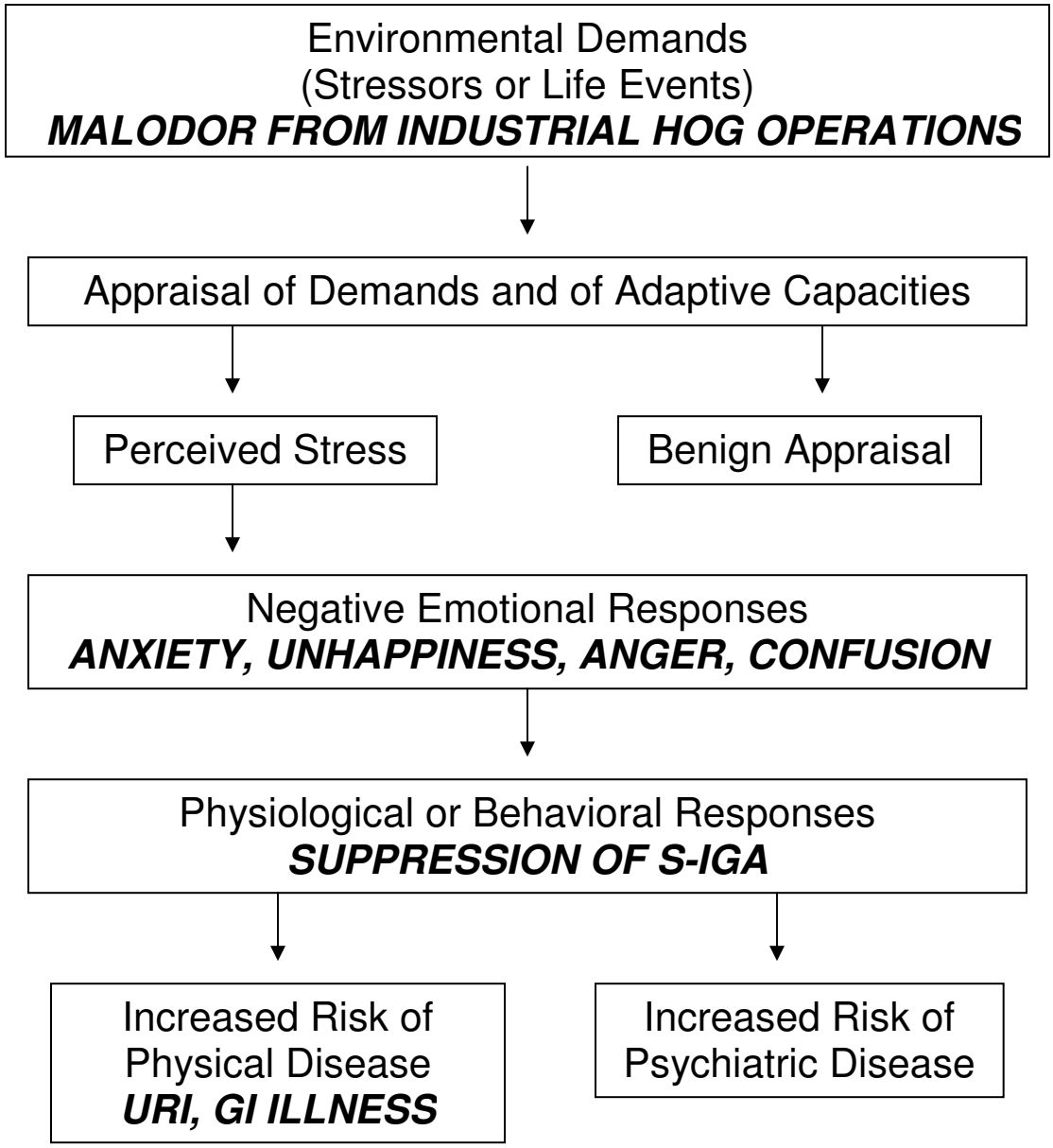
Our previous pilot study found decreased secretion of sIgA at moderate to high odor levels, specifically a decline in log sIgA secretion rate of 0.05 (SE = 0.03) for each incremental 1-unit increase in reported odor from 4 to 9 on a 9-point scale [25]. Though we did not find evidence of an overall association between odor and sIgA secretion in the current study (CHEIHO), the beta coefficients in particular subgroups (women, high John Henryism score, low butanol score) are consistent with the previous study. Moreover, the differences between subgroups in the current study are larger than the difference between the overall associations in this and the previous study. A different distribution of the various modifiers examined here may partially explain the modest differences in magnitude of the overall associations between the two studies. Variation in the results may also be partially explained by differences in the design and conduct of CHEIHO and the previous study: (a) the CHEIHO study required additional twice daily data collection activities, specifically, the collection of recall data on hourly odor exposures and the collection of blood pressure data using an automated monitor, which, if perceived as stressful, could affect a stress-mediated sIgA response; and (b) the sIgA assays were conducted at a commercial testing facility for the CHEIHO study and at UNC for the previous pilot study, so variation in sIgA secretion rates between the two studies may also be a function of differences between laboratories.

It may be that we found little evidence of an overall effect of malodor on sIgA because we found little evidence of an overall effect of stress or mood on sIgA. As depicted in Figure 4.1, we hypothesized that odor is an environmental stressor, which, when appraised

as such, may lead to a physiological effect in the form of decreased immune function. As reported in Chapter 3, we found that odor does appear to predict stress and adverse mood; ratings of stress/mood increased as ratings of odor increased, with the strongest relationship for odor as a predictor of stress. This finding, with other work by Schiffman [23], Thu (forthcoming), and Tajik (forthcoming), begins to tie the upper 4 boxes of the conceptual framework together. In this study, however, they do not appear to be linked to a physiological response.

The usefulness of sIgA in understanding health effects in neighbors of hog CAFOs is not as a marker of immune function per se, but rather as a marker of a physiological effect. With respect to future work, additional saliva samples and better specification of the timing of sample collection could improve the ability to detect a physiologic effect, if any. In a laboratory study of active and passing coping stressors on sIgA secretion, Bosch et al collected a baseline saliva sample during a rest period prior to stressor exposure, another sample during the stressor exposure, and a third sample after the stressor exposure [32]. We could consider adapting such a design for future field work. Alternatively, another marker may be preferable – perhaps cortisol, lung function, or blood pressure. sIgA varies within and between days, within and between people, for myriad reasons, and we are somewhat limited here by our reductionist approach [51], trying to isolate a single predictor of a single, specific physiological parameter. The effects of emissions from hog CAFOs on the health and quality of life of neighbors are wide-ranging, and future research could be more effective if it were less narrow in its approach.

Figure 4.1*



* Adapted from Cohen, S., R. Kessler, and L. Gordon, *Strategies for measuring stress in studies of psychiatric and physical disorders*, in *Measuring Stress: A Guide for Health and Social Scientists*, S. Cohen, R. Kessler, and L. Gordon, Editors. 1997, Oxford University Press: New York.

Table 4.1. Variable coding for Independent Variables and Covariates.

	Variable Coding
Independent Variables	
Odor	0 = 0-5 1 = 6 2 = 7 3 = 8
Stressed or annoyed Nervous or anxious Gloomy, blue, or unhappy Angry, grouchy, or bad-tempered Confused or unable to concentrate	0 = 0-4 1 = 5-8
Covariates	
Time Dependent	
Time of day	0 = morning 1 = evening
Study day	Linear term
Study week	0 = 2^{nd} week + 1 = 1^{st} week
Cold, flu, or stomach flu	0 = no cold or flu 1 = any cold or flu
ENT irritation or cough	0 = no irritation 1 = any irritation
Time Independent	
Gender	0 = male 1 = female
Age, median = 55.5 years	0 = age $\leq$ 55.5 years 1 = age > 55.5 years
Mastery, median = 40	0 = score < 40 1 = score $\geq$ 40
John Henryism, median = 52	0 = score < 52 1 = score $\geq$ 52
Odor threshold, median = 40 ppm	0 = threshold $\leq$ 40 ppm 1 = threshold > 40 ppm

Figure 4.2

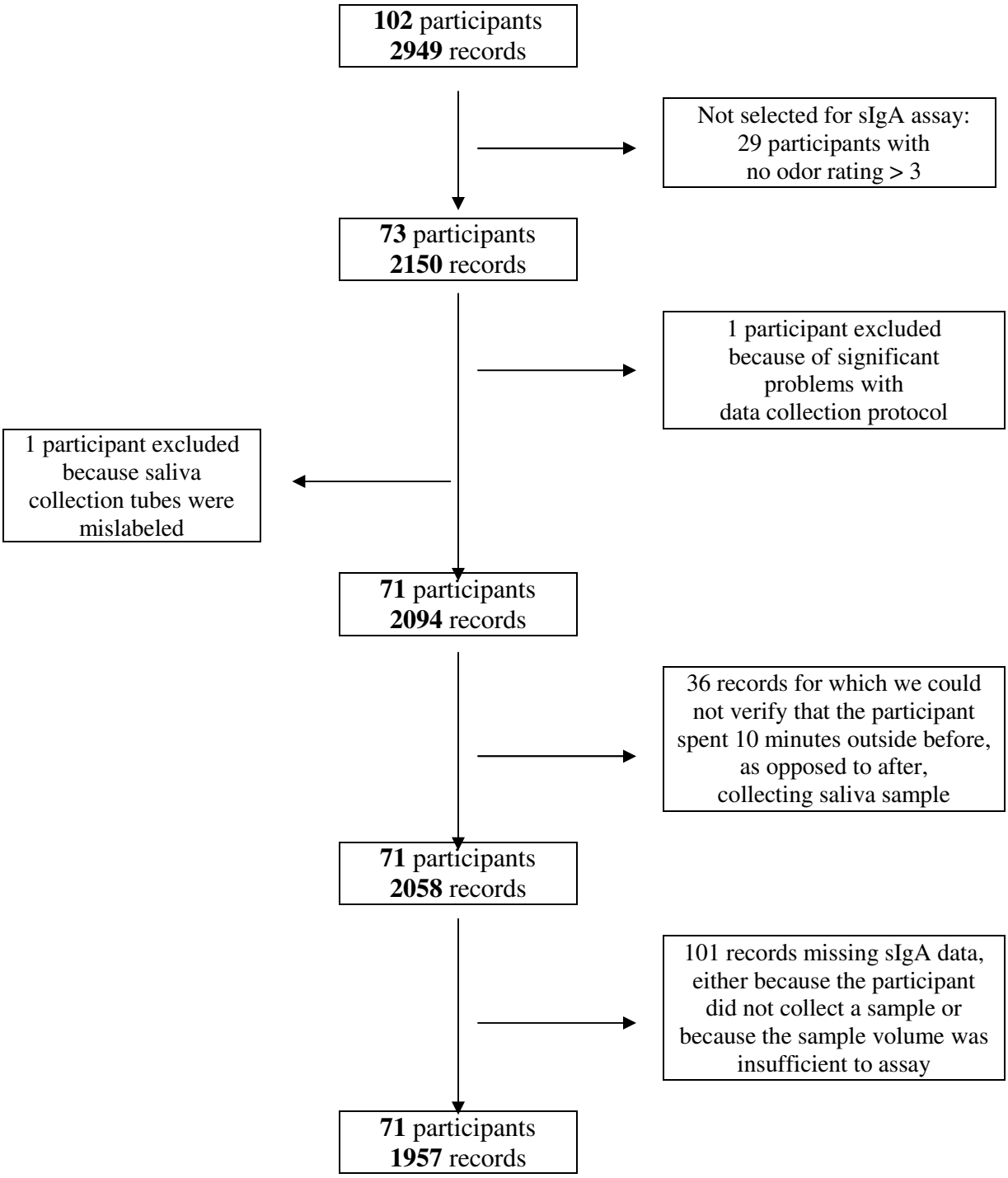

102 participants
2949 records
Not selected for sIgA assay:
29 participants with
no odor rating > 3
73 participants
2150 records
1 participant excluded
because of significant
problems with
data collection protocol
1 participant excluded
because saliva
collection tubes were
mislabeled
71 participants
2094 records
36 records for which we could
not verify that the participant
spent 10 minutes outside before,
as opposed to after,
collecting saliva sample
71 participants
2058 records
101 records missing sIgA data,
either because the participant
did not collect a sample or
because the sample volume was
insufficient to assay
71 participants
1957 records

Table 4.2. Characteristics of Participants in the CHEIHO study.

	n records	N participants
Age		
> 55.5 years	1013	36
≤ 55.5 years	944	35
Gender		
Female	1325	49
Male	632	22
Race		
Black	1568	59
Not black[a]	389	12
Grew up around livestock		
Yes	1511	55
No	366	13
Missing	80	3
Total	*1957*	*71*

[a] 11 white participants and 1 Latino participant

Figure 4.3. Distribution of sIgA Secretion Rate Across Time Points.

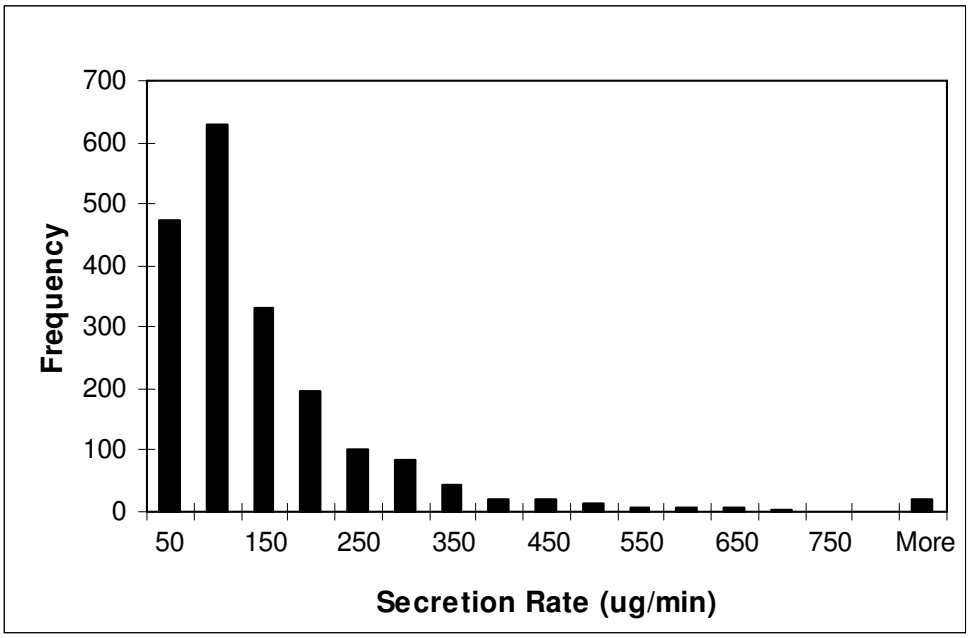


Table 4.3. Number (%) of Records, n, and Number of Participants, N, in Each Category of the Independent Variables.

	Odor Rating			Stressed or Annoyed?			Nervous or Anxious?			Gloomy, Blue, or Unhappy?			Angry, Grouchy or Bad-tempered?			Confused or Unable to Concentrate?		
Level	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**	**N**
0	767	39.2	60	1412	72.2	68	1557	79.6	70	1605	82.0	69	1730	88.4	70	1753	89.6	70
1	345	17.6	59	288	14.7	51	218	11.1	34	188	9.6	36	109	5.6	33	104	5.3	22
2	216	11.0	56	101	5.2	37	85	4.3	22	33	1.7	14	22	1.1	9	28	1.4	7
3	180	9.2	57	52	2.7	22	35	1.8	12	46	2.4	14	11	0.6	7	11	0.6	5
4	118	6.0	45	14	0.7	10	9	0.5	2	11	0.6	6	5	0.3	4	8	0.4	3
5	69	3.5	39	18	0.9	12	5	0.3	5	9	0.5	5	14	0.7	8	2	0.1	2
6	104	5.3	39	19	1.0	10	1	0.1	1	9	0.5	5	10	0.5	4	1	0.1	1
7	22	1.1	11	6	0.3	4	1	0.1	1	6	0.3	3	4	0.2	2	0	0.0	0
8	25	1.3	12	7	0.4	5	1	0.1	1	5	0.3	3	8	0.4	3	0	0.0	0
Missing	111	5.7	33	40	2.0	19	45	2.3	19	45	2.3	22	44	2.3	20	50	2.6	21
Total	*1957*	*100.0*	*71*	*1957*	*100.0*	*71*	*1957*	*100.0*	*71*	*1957*	*100.0*	*71*	*1957*	*100.0*	*71*	*1957*	*100.0*	*71*

Table 4.4. Associations Between sIgA Secretion Rate and Odor Reported After Prescribed 10-Minute Outdoor Exposure, Stratified by Modifiers[a]

	β	SE	95% CI
Odor rating (0-5, 6,7,8)			
All records	-0.03	0.03	(-0.09 – 0.04)
Morning	0.04	0.06	(-0.07 – 0.15)
Evening	-0.06	0.04	(-0.14 – 0.02)
Male	0.08	0.06	(-0.04 – 0.21)
Female	-0.07	0.04	(-0.15 – 0.01)
Low mastery	-0.06	0.04	(-0.15 – 0.03)
High mastery	0.03	0.05	(-0.07 – 0.13)
Low John Henryism	0.07	0.05	(-0.02 – 0.17)
High John Henryism	-0.12	0.05	(-0.21 – -0.02)
Low butanol score	-0.10	0.04	(-0.18 – -0.02)
High butanol score	0.12	0.06	(0.01 – 0.24)
No irritation reported	-0.06	0.06	(-0.18 – 0.07)
Any irritation reported	-0.01	0.04	(-0.09 – 0.07)

[a] With the intercept and time of day (0=morning, 1=evening) included as random effects

Table 4.5. Associations Between sIgA Secretion Rate and Reported Stress/Mood, with Reported Stress Stratified by Modifiers[a]

	β	SE	95% CI
(a) Stressed or annoyed? (0-4, 5-8)	-0.12	0.10	(-0.31 – 0.07)
Morning	0.06	0.14	(-0.21 – 0.33)
Evening	-0.29	0.13	(-0.55 – -0.032)
≤ 55.5 years	0.08	0.15	(-0.22 – 0.38)
> 55.5 years	-0.25	0.12	(-0.49 – -0.01)
Low mastery	-0.17	0.13	(-0.43 – 0.10)
High mastery	-0.07	0.14	(-0.34 – 0.19)
Low John Henryism	-0.23	0.17	(-0.56 – 0.11)
High John Henryism	-0.07	0.12	(-0.30 – 0.16)
(b) Nervous or anxious? (0-4, 5-8)	-0.23	0.21	(-0.65 – 0.18)
(c) Gloomy, blue, or unhappy? (0-4, 5-8)	-0.13	0.13	(-0.37 – 0.12)
(d) Angry, grouchy, or bad-tempered? (0-4, 5-8)	-0.25	0.12	(-0.49 – -0.003)
(e) Confused or unable to concentrate? (0-4, 5-8)	-0.13	0.34	(-0.80 – 0.54)

[a] With the intercept and time of day (0=morning, 1=evening) included as random effects

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CHAPTER 5

CONCLUSIONS

In North Carolina, and throughout the United States, pork production has become industrialized over the last 20 years, with the majority of hogs now raised in confinement houses and their waste stored either beneath the confinement houses or in open-air lagoons until it is sprayed via irrigation systems on nearby fields as fertilizer [1, 2]. People living near these industrial farms describe frequent exposure to malodor and adverse effects on their health and quality of life. A number of studies have documented adverse health effects in neighbors of industrial hog operations. [3-16]

The earliest survey [15], conducted in Iowa, identified symptoms reported in excess by participants living within 2 miles of an IHO, grouped into the following 4 clusters: (1) respiratory symptoms, (2) nausea, weakness, dizziness, and fainting, (3) headaches and plugged ears, and (4) burning eyes, runny nose and throat. In North Carolina, Wing and Wolf observed that participants living near an industrial hog operation reported more frequent headaches, runny nose, sore throat, excessive coughing, diarrhea, and burning eyes than did residents of the community with no intensive livestock operations [16]. A second survey conducted in North Carolina by Bullers [4] documented higher frequencies of the same sets of symptoms reported by neighbors of IHOs, relative to frequencies reported by controls.

A number of studies have documented excess symptom reports in communities around other malodor-producing industrial facilities, including solid and hazardous waste facilities, petroleum refineries, manufacturing facilities, and landfills [17-22]. Given presumably low levels of exposure to toxic pollutants downwind from malodorous industrial facilities, several authors have postulated non-toxicologic hypotheses to explain symptom reporting [20, 21, 23]. Posited causal mechanisms include (1) an odor-mediated response, "innate odor aversions, exacerbation of underlying medical conditions, and conditioned responses to odors after traumatic chemical overexposures", and (2) a stress-mediated response in which odor triggers symptoms via stress or activation of the autonomic nervous system. [21]

In exploring potential mechanisms through which odor may affect the health of neighbors, I evaluated the hypothesis that malodor from IHOs has a psychophysiologically mediated effect on the secretory immune system. Specifically, I considered whether (a) reported odor was associated with stress and/or adverse mood and (b) reported odor and/or stress were associated with decreased secretion of sIgA. The data came from a collaborative community-based participatory research study, Community Health Effects of Industrial Hog Operations (CHEIHO), which combined both quantitative and qualitative methods of data collection.

The design of the CHEIHO study permitted improvement of design limitations of previous studies of the health effects in neighbors of IHOs. I had the opportunity to use incident, rather than prevalent, data. I also analyzed an objective measure of a physiologic effect of exposure, sIgA. I did use self-reported data on odor, stress, and mood; however, because I chose to investigate a psychophysiological hypothesis, the participants' perceptions

of odor and its effect on their mental health were relevant. A further improvement was the longitudinal design which permitted each person to serve as his/her own control, whereas previous work utilized external controls [4, 14-16].

Odor, Stress, and Mood

In evaluating whether people exposed to malodor did indeed perceive such exposure as stressful, I found that ratings of feeling stressed/annoyed, nervous/anxious, gloomy/unhappy, angry/grouchy, and confused/unable to concentrate increased with ratings of malodor. Of the 5 outcome variables, odor was most strongly related to stress/annoyance. Age and John Henryism score appeared to be modifiers of that relationship, with older people and those with higher John Henryism scores more affected by malodor. Time of day was a potential modifier, with the odor effect somewhat diminished in the evenings compared to mornings. These findings are consistent with a large literature on malodor as an environmental stressor [20, 21, 24-31], though the results on age and coping as modifiers are mixed [24, 25, 29-31]. Findings were also consistent with the only other known study of the effect on mood, where the authors found significantly increased tension, depression, anger, fatigue, confusion, and less vigor reported by neighbors when malodor was present [14].

An important design limitation was the contemporaneous assessment of both exposure and outcome. Because both exposure and outcome were assessed contemporaneously, by self-report, it is difficult to determine how the assessment of one affected the assessment of the other. Participants spent 10 minutes outdoors before returning indoors to complete the required data collection activities; they rated the intensity of any

malodor present and then rated any stress and/or adverse mood. If an odor were present, and if it had an effect on the participant's stress/mood, s/he rated both odor and stress/mood while experiencing that stress, annoyance, and negative mood. Rating the odor while stressed or annoyed, for example, may have induced a higher rating than the participant would have rated in the absence of feeling stressed or annoyed.

Odor, Stress, and Secretory Immune Function

I found little evidence of an overall association between sIgA secretion rate and malodor from hog CAFOs. There was a suggestion of an effect at the highest levels of reported odor and confined to particular subgroups of the study population (women, high John Henryism score, low butanol score). The observed effect of reported stress on sIgA secretion, if any, was also confined to particular subgroups (older people, low John Henryism score). Of the four mood variables we evaluated, feeling angry, grouchy, or bad-tempered appeared to have an effect on sIgA secretion, but that was largely attributable to a single influential participant. Feeling nervous or anxious did not have an effect in the full study population but did appear to have an effect if the influential participant was excluded.

It may be that we found little evidence of an overall effect of malodor on sIgA because we found little evidence of an overall effect of stress or mood on sIgA. As depicted in Figure 1.1, we hypothesized that odor is an environmental stressor, which, when appraised as such, may lead to a physiological effect in the form of decreased immune function. Our results on malodor as a predictor of stress and negative mood, together with other work by Schiffman [23], Thu (forthcoming), and Tajik (forthcoming), begins to tie the upper 4 boxes

of the conceptual framework together. In this study, however, they do not appear to be linked to a physiological response. It is possible that some combination of unmeasured time-dependent confounders, unmeasured time-independent modifiers, and/or measurement error affected the results. It is also possible that the saliva collection protocol failed to capture the appropriate information at the appropriate time relative to exposure to the stressor (see below).

Future Studies

Though malodor was strongly associated with stress and mood, it is problematic that both exposure and outcome were assessed by self-report. Steinheider et al [29-31] addressed this problem by using a team of trained odor monitors to systematically rate industrial odors over the course of 6 months in neighborhoods surrounding the source. This provides an independent assessment of odor, but it does not take into account the fact that people perceive odors differently and that perception may affect their physiological response. Though labor intensive, future work could nonetheless consider a similar system. Also possible are objective assessments of stress and/or annoyance. Cortisol and autonomic nervous system activation could be evaluated [32, 33]. There is also work suggesting assessment of the startle reflex and breathing changes as physiological indicators of annoyance [34].

With respect to future work on sIgA as a physiologic marker of exposure, additional saliva samples and better specification of the timing of sample collection could improve the ability to detect an effect, if any. In a laboratory study of active and passing coping stressors

on sIgA secretion, Bosch et al collected a baseline saliva sample during a rest period prior to stressor exposure, another sample during the stressor exposure, and a third sample after the stressor exposure [32]. We could consider adapting such a design for future field work. Alternatively, future work could consider cortisol, a direct physiological marker of stress [32], instead of a downstream marker such as sIgA. Lung function and blood pressure could be considered as well, particularly since they are more explicit measures of adverse health effects. Trying to isolate the effect of odor and/or reported stress on sIgA, a single predictor of a single, specific physiological parameter, is somewhat reductionistic [35] and limits the scope of potential adverse health effects. Future research could be more effective if it were less narrow in its approach.

In sum, I observed evidence of odor as a stressor but limited evidence of an acute effect of either reported odor or stress on sIgA secretion. Several studies have noted increased symptom reports by neighbors of IHOs [4, 15, 16]. However, the mechanism through which low-level emissions affect physical health symptoms remains unexplained by this or other studies.

Public Health Significance

Malodor itself, from IHOs and from other polluting industrial facilities, is an important public health problem, with well-documented effects on stress/annoyance and quality of life [4, 5, 10, 16, 17, 19, 22, 24, 29-31, 36-40]. Neighbors of solid waste facilities and a petroleum refinery, for example, describe similar effects on quality of life as do neighbors of IHOs. They express concern about water pollution, property values, traffic, and

pests, about odors which prevent them from enjoying the outdoors, from hanging clothes outside to dry. Like CAFO neighbors, they employ similar strategies to cope with odors, including closing windows, keeping the house closed up, and staying indoors. Neighbors also express distrust of corporations and government and the influence of money. They express the desire to be able to raise their children in a small town with fresh air. [19, 38] Malodor affects health, defined broadly as more than the absence of disease.

In North Carolina, neighbors of IHOs are more likely to be poor and/or nonwhite [41]. Exposure to malodor is inequitable. If the results of the suggested effect of malodor on stress/mood are generalizable, they likely affect a population already exposed to the economic stress associated with poverty and/or stress associated with the experience of racism. Here, I found little evidence of a physiologic effect of malodor on secretory immune function; however, given (a) the impact of malodor on reported physical health, mental health, and quality of life and (b) the injustice of exposure, further work is important.

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Community Health Effects of Industrial Hog Operations

Why is the study being done?

This research will monitor air emissions and the presence of odors in communities surrounding industrial hog operations in eastern North Carolina. At the same time, people living in the same area will be asked about symptoms of physical health problems and variations in moods that they may be experiencing. This study will also examine whether the presence of odor affects blood pressure, the immune system and respiratory function. Immune function will be assessed by analyzing saliva. Lung function will be measured by breathing into a small, hand-held meter; blood pressure by an easy-to-use digital instrument.

Who is eligible to participate in the study?

You are eligible:

- If you live within 1-2 miles of an industrial hog operation
- If you are 18 years or older
- If you are able and willing to spend about 40-45 minutes each day for 14 days in data collection activities
- If you do not smoke cigarettes, cigars or a pipe.

How many people will take part in the study?

We will identify 10-12 communities where 5-10 persons in each community want to participate. More than one adult in each household can participate.

How long will I participate in the study?

Your participation in the study will last for two weeks (14 consecutive days).

Does it cost anything to be in the study?

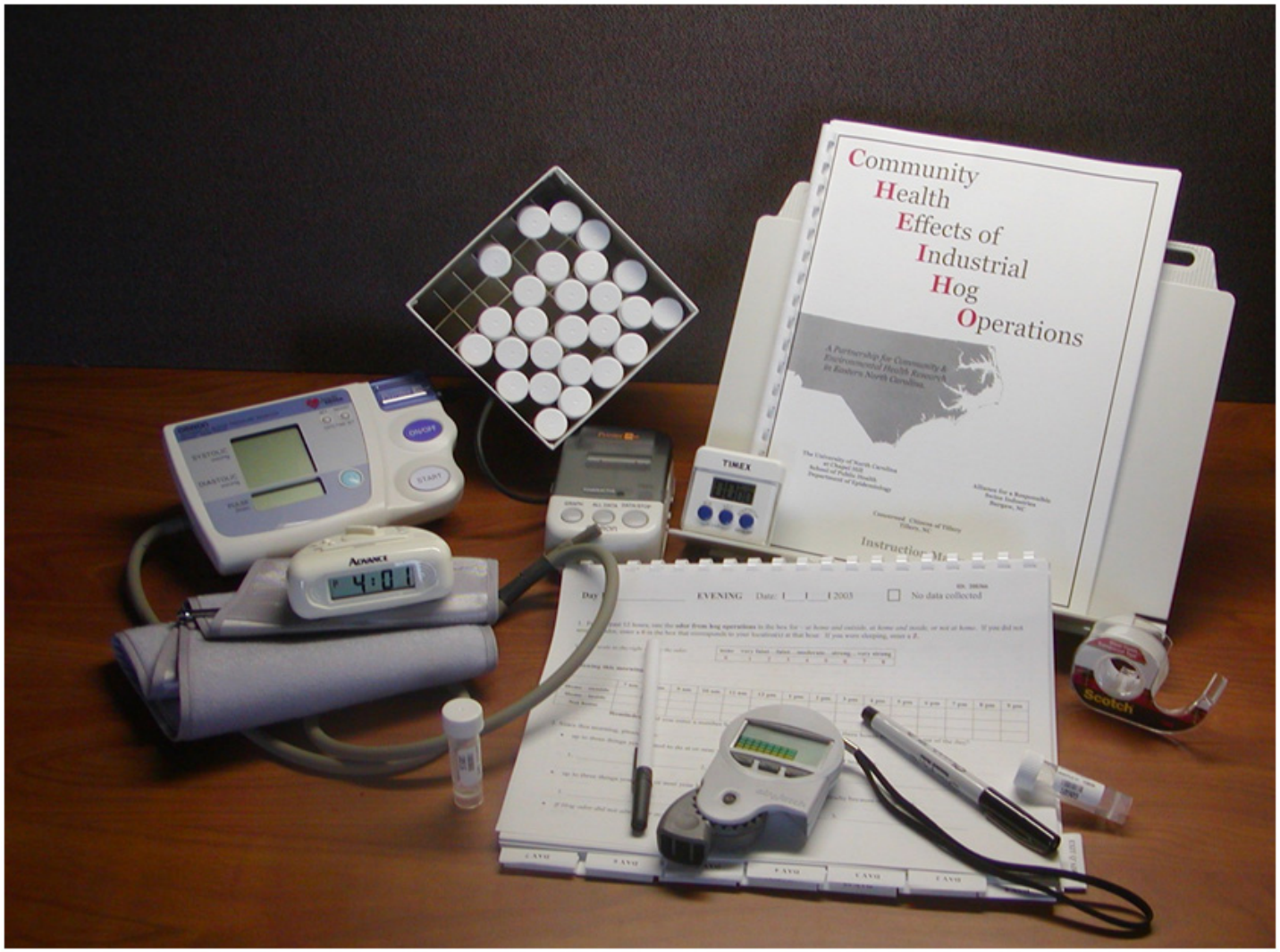
There are no financial costs to you. You will be required to attend a training session for instructions on how to complete data collection activities. Each day you participate in the study you will be required to spend about 40-45 minutes in data collection activities. You will be given $100 each week of participation and a $50 bonus if you complete all data collection activities for 14 days.

What will the study involve if I decide to participate?

- At the beginning of the study you will be asked to complete a brief questionnaire about specific health problems that you may have, regular medication usage, and characteristics about you and your home.
- Each day you will be asked to go outside at two specific times (once in the morning and again in the evening - about 12-14 hours later) for 10 minutes to smell for hog odors.
- After sitting outside for 10 minutes you will be asked to:
  - write down whether there is an odor and how strong it is.
  - note physical signs and symptoms that you may have experienced.
  - check your blood pressure with an easy-to-use instrument.
  - provide a saliva sample for immune function.
  - blow into a meter to test your lung function.
  - report how you felt during the day.

Appendix 2: CHEIHO Environmental Monitoring Equipment

Appendix 3: Data Collection Material Used by Study Participants



Appendix 4. Associations Between sIgA Secretion Rate and Odor Reported After Prescribed 10-Minute Outdoor Exposure, With and Without Influential Participant[a]

	All study participants (N=71)			Influential participant excluded (N=70)		
	β	SE	95% CI	β	SE	95% CI
Odor rating (0-5, 6,7,8)	-0.03	0.03	(-0.09 – 0.04)	0.01	0.03	(-0.06 – 0.08)
Morning	0.04	0.06	(-0.07 – 0.15)	0.06	0.06	(-0.06 – 0.17)
Evening	-0.06	0.04	(-0.14 – 0.02)	-0.02	0.04	(-0.10 – 0.07)
Male	0.08	0.06	(-0.04 – 0.21)	0.09	0.06	(-0.03 – 0.20)
Female	-0.07	0.04	(-0.15 – 0.01)	-0.03	0.04	(-0.11 – 0.05)
Low mastery	-0.06	0.04	(-0.15 – 0.03)	0.003	0.05	(-0.09 – 0.10)
High mastery	0.03	0.05	(-0.07 – 0.13)	0.03	0.05	(-0.07 – 0.13)
Low John Henryism	0.07	0.05	(-0.02 – 0.17)	0.07	0.05	(-0.02 – 0.17)
High John Henryism	-0.12	0.05	(-0.21 – -0.02)	-0.07	0.05	(-0.17 – 0.03)
Low butanol score	-0.10	0.04	(-0.18 – -0.02)	-0.06	0.04	(-0.15 – 0.03)
High butanol score	0.12	0.06	(0.01 – 0.24)	0.12	0.06	(0.01 – 0.23)
No irritation reported	-0.06	0.06	(-0.18 – 0.07)	-0.06	0.06	(-0.17 – 0.06)
Any irritation reported	-0.01	0.04	(-0.09 – 0.07)	0.05	0.05	(-0.04 – 0.14)

[a] With the intercept and time of day (0=morning, 1=evening) included as random effects

Appendix 5. Associations Between sIgA Secretion Rate and Reported Stress/Mood, With and Without Influential Participant[a]

	All study participants (N=71)			Influential participant excluded (N=70)		
	β	SE	95% CI	β	SE	95% CI
(a) Stressed or annoyed? (0-4, 5-8)	-0.12	0.10	(-0.31 – 0.07)	-0.09	0.10	(-0.28 – 0.11)
Morning	0.06	0.14	(-0.21 – 0.33)	-0.05	0.15	(-0.34 – 0.24)
Evening	-0.29	0.13	(-0.55 – -0.032)	-0.12	0.13	(-0.38 – 0.15)
Younger	0.08	0.15	(-0.22 – 0.38)	0.08	0.15	(-0.21 – 0.37)
Older	-0.25	0.12	(-0.49 – -0.01)	-0.23	0.14	(-0.50 – 0.04)
Low mastery	-0.17	0.13	(-0.43 – 0.10)	-0.11	0.16	(-0.41 – 0.20)
High mastery	-0.07	0.14	(-0.34 – 0.19)	-0.07	0.13	(-0.33 – 0.18)
Low John Henryism	-0.23	0.17	(-0.56 – 0.11)	-0.22	0.16	(-0.54 – 0.10)
High John Henryism	-0.07	0.12	(-0.30 – 0.16)	-0.002	0.13	(-0.25 – 0.25)
(b) Nervous or anxious? (0-4, 5-8)	-0.23	0.21	(-0.65 – 0.18)	-0.38	0.21	(-0.80 – 0.04)
(c) Gloomy, blue, or unhappy? (0-4, 5-8)	-0.13	0.13	(-0.37 – 0.12)	-0.09	0.13	(-0.35 – 0.17)
(d) Angry, grouchy, or bad-tempered? (0-4, 5-8)	-0.25	0.12	(-0.49 – -0.003)	-0.06	0.14	(-0.34 – 0.22)
(e) Confused or unable to concentrate? (0-4, 5-8)	-0.13	0.34	(-0.80 – 0.54)	-0.13	0.33	(-0.76 – 0.51)

[a] With the intercept and time of day (0=morning, 1=evening) included as random effects