Association Among Acrylamide, Blood Insulin, and Insulin Resistance in Adults

Chien-Yu Lin, md, mph[1,2,3]
Yu-Chuan Lin, md[2,4]
Hsu-Ko Kuo, md, mph[5]
Juey-Jen Hwang, md, phd[5]

Jiunn-Lee Lin, md, phd[5]
Pau-Chung Chen, md, phd[2]
Lian-Yu Lin, md, phd[5]

OBJECTIVE — Exposure to acrylamide in foodstuffs and smoking has become a worldwide concern. The effect of acrylamide on glucose homeostasis is not known. The goal of the present study was to test the hypothesis that trace acrylamide exposure might be independently associated with both reduced blood insulin and reduced insulin resistance.

RESEARCH DESIGN AND METHODS — We examined 1,356 participants with reliable measures of glucose homeostasis and Hb adducts of acrylamide (HbAA) and glycidamide from the National Health and Nutrition Examination Survey, 2003–2004. Glucose homeostasis was assessed by the measurement of plasma glucose, serum insulin, and the homeostasis model assessment of insulin resistance (HOMA-IR).

RESULTS — In a linear regression model, a 1-unit increase in log HbAA was associated with a decrease in serum insulin (β coefficient $= -0.20 \pm 0.05$, $P = 0.001$) and HOMA-IR (β coefficient $= -0.23 \pm 0.05$, $P < 0.001$). After HbAA concentrations were divided into quartiles in the fully adjusted models, the adjusted serum insulin level and HOMA-IR significantly decreased across quartiles of HbAA ($P_{trend} < 0.001$ for both). In subgroup analysis, the association of HbAA levels with HOMA-IR and insulin levels was stronger in subjects who were white or had ever smoked or in subjects with a lower education level or a BMI <25 or >30 kg/m^2.

CONCLUSIONS — Acrylamide is associated with reduced serum insulin levels in adults. Further clinical and animal studies are warranted to clarify the putative causal relationship.

A crylamide, a highly reactive α,β-unsaturated carbonyl compound, is widely used to synthesize polymers for industrial applications such as soil conditioning, wastewater treatment, research applications, cosmetics, and the paper and textile industries (1). Besides industrial and laboratory uses, acrylamide in foodstuffs has become a worldwide concern because of its generation in a variety of fried and oven-baked foods during cooking. Attention was drawn to this fact initially by Tareke et al. (2) in 2002, and subsequent biochemical anal-

ysis showed that heating of free amino acids (asparagines) and sugars during food processing at 248°F (120°C) resulted in the formation of acrylamide concentrations of up to 1 mg/kg food (3). According to recent data, the mean daily workplace inhalation exposure is 1.4–18.6 µg/kg body wt (4), whereas human consumption via food is about 1 µg · kg body wt^{-1} · day^{-1} in the general population and 4 µg · kg body wt^{-1} · day^{-1} in high consumers (5). Moreover, acrylamide is a component of cigarette smoke. Its content has been estimated at 1.1–2.34 µg/cigarette, which is

clearly an important source of acrylamide exposure (6).

The majority of acrylamide is conjugated with glutathione in the human body, and some (about 15%) is activated by cytochrome P450 CYP2E1 to a reactive epoxy compound, glycidamide. Glycidamide is subsequently metabolized by hydrolysis and conjugated with glutathione. Acrylamide and glycidamide form adducts with the NH$_2$-terminal NH$_2$ group of the valine residue of Hb (7). Hb adducts reflect an integrated concentration over 4 months (8); therefore, these adducts are useful as predictors of toxicity. Hb adducts of acrylamide (HbAA) and glycidamide (HbGA) have been used as biomarkers of exposure and to estimate the internal dose from workplace exposure as well as in the general population (9).

The biological consequences of acrylamide exposure have chiefly centered on neurotoxicity ever since this effect was observed in humans exposed to this compound in the workplace (9). Subsequently, experimental exposure of rodents to acrylamide has shown impaired development, reproductive toxicity, genotoxicity, and carcinogenicity. However, epidemiological studies in the workplace and general population have not established an unambiguous link between acrylamide exposure and human cancer (9–11). Acrylamide was classified by the International Agency for Research on Cancer as a probable human carcinogen (12). Given the lack of dose-response data for human neurotoxicity, the risk assessment was based on rodent studies and supported by primate studies of acrylamide neuropathy. Based on these data, the World Health Organization in 2005 concluded that the "no observed effect level" for acrylamide neuropathy is 0.2 mg · kg body wt^{-1} · day^{-1} (5). This provides a margin between exposure and the no observed effect level of 200. Therefore, it is not likely that acrylamide-induced neurotoxicity will be detected in the general population.

A recent study, using an animal model, showed both lower insulin and triglyceride concentrations after continuous intake of trace acrylamide in a dose of 0.28 ppm similar to that for the general population (13). In another study, rats

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treated with acrylamide at relatively low doses demonstrated diminished appetitive motivation (14). In a recent cross-sectional epidemiology study in Europe, HbAA was inversely associated with BMI in smokers (15). Based on these studies, we hypothesized that trace acrylamide exposure might be independently associated with reduced insulin resistance and improved serum lipid profiles. Because the homeostasis model assessment for insulin resistance (HOMA-IR) is a reliable surrogate measure of insulin resistance (16), we can use fasting glucose and insulin concentrations to accurately estimate insulin resistance status. The goal of the present study was to test this hypothesis by examining data from the National Health and Nutrition Examination Survey (NHANES) collected from 2003 to 2004.

RESEARCH DESIGN AND METHODS

— Data were from NHANES 2003–2004. The NHANES is a population-based survey designed to collect information on the health and nutrition of the U.S. household population and to obtain a representative sample of the noninstitutionalized civilian U.S. population. The survey data are released every 2 years. Detailed survey operations manuals, consent documents, and brochures of the NHANES 2003–2004 are available on the NHANES Web site (17). We limited our analyses to the 6,990 participants aged at least 20 years who had a test for HbAA and HbGA. Among these subjects, only 3,169 had a morning examination and measurements of fasting plasma glucose and serum insulin. Of these participants, 1,356 subjects without missing data were included in the final analyses.

Anthropometric and biochemical data

According to the statements on the NHANES Web site, data were collected at all study sites by trained personnel using standardized procedures. Sociodemographic and medical information such as age, sex, race/ethnicity, education level, household income, and medication usage were collected during the household interview. Alcohol intake was recorded and determined by the questionnaire and categorized into three levels (<12 drinks, <144 drinks, and ≥144 drinks per year). Smoking status was categorized as active smoker, former smoker, and nonsmoker by a questionnaire on smoking (18). We also quantified smoking status by serum

cotinine levels (<0.1, 0.1–10, or ≥10 ng/ml) in the same manner as in a previous study (19). BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured at the iliac crest to the nearest 0.1 cm. Laboratory measurements were performed in a mobile examination center. For serum markers, blood specimens were collected by glass tubes (red-top Vacutainer), whereas for plasma glucose, blood specimens were collected in a vacuum tube containing sodium fluoride (gray-top Vacutainer). Blood specimens were processed locally and then were stored and shipped to central laboratories for analysis. Levels of serum total cholesterol and triglyceride were measured enzymatically. Levels of HDL cholesterol were measured after precipitation of other lipoproteins on a Hitachi model 704 analyzer (Roche Diagnostics, Indianapolis, IN). Plasma glucose was measured by the hexokinase enzymatic method (Cobas Mira Chemistry System; Roche Diagnostic Systems, Montclair, NJ). Serum C-reactive protein levels were measured by latex-enhanced nephelometry (Dade Behring Nephelometer II Analyzer System; Dade Behring Diagnostic, Somerville, NJ). Cotinine was measured in serum samples using isotope-dilution high-performance liquid chromatography/atmospheric pressure chemical ionization tandem mass spectrometry (Hewlett-Packard model 1090L high-performance liquid chromatograph and PE-Sciex API III triple quadrupole mass spectrometer) (20). GHb was measured by a boronate affinity high-performance liquid chromatography system and converted to A1C levels (automated high-performance liquid chromatography system, model CLC330; Primus, Kansas City, MO.). Serum insulin was determined by immunoenzymatic assay with Tosoh AIA-PACK immunoreactive insulin. The HOMA-IR, the product of basal glucose and insulin levels divided by 22.5, was used as a reliable surrogate measure of insulin resistance (16).

Assessment of HbAA and HbGA

Human whole blood or erythrocytes were used to measure HbAA and HbGA. Specifically, the reaction products with the NH_2-terminal valine of the Hb protein chains (*N*-[2-carbamoylethyl] valine and *N*-[2-hydroxycarbamoyl-ethyl] valine for acrylamide and glycidamide adducts, respectively) were measured. This method is based on a modified Edman reaction,

which uses the formation of Edman products from *N*-alkylated amino acids in neutral or alkaline conditions rather than the acidic conditions required in the conventional Edman reaction (21). This optimized method was further refined and modified to increase the sensitivity and enable automation. HbAA and HbGA were quantified using octapeptides with the same amino acid sequence as the NH_2 terminus of the β-chain of Hb and with acrylamide and glycidamide attached at the valine residue (AA-VHLTPEEK, GA-VHLTPEEK); the corresponding stable isotope-labeled AA-Val(13C5 15N)-HLTPEEK was used as an internal standard. Total Hb was measured using calibrators provided with the manufacturer's assay kit (22). The limit of detection was 2 pmol/g Hb for HbAA and 3 pmol/g Hb for HbGA. For concentrations below the detection limits (only 0.07 and 2.2% of blood samples, respectively), a value was assigned by NHANES that we used in our analyses.

Statistics

Data are expressed as means ± SE. Continuous variables were compared between groups by an unpaired Student *t* test, whereas categorical variables were compared by a χ^2 test. The strength of the associations between the concentrations of HbAA, HbGA, and plasma glucose homeostatic markers was tested using linear regression models.

For linear regression models, we used an extended model approach for covariates to adjust for potential confounders. Model 1 was adjusted for age, sex, and race; model 2 was adjusted for age, sex, race, smoking status, alcohol intake, education levels, household income, BMI, A1C, and insulin/glucose/HOMA-IR. When the plasma glucose was treated as an independent variable, serum insulin was entered as a dependent variable and vice versa. When the independent variables were the derivatives of the plasma glucose and the serum insulin, both the plasma glucose and the serum insulin were not adjusted in the model. The HOMA-IR was adjusted in the final model if the independent variable was not an arithmetic combination of the plasma glucose and the serum insulin. The relative contribution of each dependent variable to predict the variation of dependent variable was determined by partial R^2. Log transformation was performed for vari-

Table 1—Acrylamide adducts and glycidamide adducts concentrations by participant characteristics

	No. (weighted %)	HbAA (pmol/g Hb)	P*	HbGA (pmol/g Hb)	P*
Overall	1,356 (100)	61.6 (57.4–66.0)		57.4 (54.0–61.6)	
Age			0.002		<0.001
20–39 years	494 (39.3)	66.7 (61.0–73.0)		63.4 (59.2–68.7)	
40–59 years	401 (40.2)	62.8 (56.3–70.1)		59.2 (55.7–62.8)	
≥60 years	461 (20.5)	51.4 (47.5–55.2)		45.2 (39.7–51.9)	
Sex			0.003		0.551
Men	660 (48.7)	65.4 (59.7–71.5)		57.4 (54.1–61.0)	
Women	696 (51.3)	58.0 (54.6–62.2)		58.0 (53.0–62.8)	
Race			0.065		0.712
Mexican American	279 (8.1)	63.4 (59.7–75.2)		61.6 (55.2–68.7)	
Non-Hispanic white	732 (73.2)	62.2 (57.4–67.4)		58.0 (53.0–62.8)	
Non-Hispanic black	245 (9.9)	66.7 (58.6–75.2)		56.3 (51.4–61.6)	
Others	100 (8.8)	50.9 (42.1–61.6)		54.1 (48.4–60.3)	
Smoking			<0.001		<0.001
Nonsmoker	888 (63.0)	49.4 (46.5–52.0)		48.4 (45.2–51.9)	
Former smoker	189 (13.3)	52.5 (45.6–59.7)		48.9 (41.7–56.8)	
Active smoker	279 (23.7)	124.0 (108.9–141.2)		98.5 (89.1–110.0)	
Cotinine			<0.001		<0.001
<0.1 ng/ml	736 (50.1)	47.5 (45.2–49.9)		47.0 (43.0–50.9)	
0.1–10 ng/ml	264 (20.2)	50.4 (44.3–56.8)		49.9 (43.4–56.8)	
≥10 ng/ml	356 (29.7)	110.0 (99.5–121.5)		90.0 (83.1–97.5)	
Alcohol drinking status			0.053		0.601
<12 drinks/year	681 (44.9)	56.8 (51.9–62.2)		57.4 (52.5–62.8)	
<144 drinks/year	325 (26.8)	61.0 (54.6–67.4)		58.0 (51.4–64.7)	
≥144 drinks/year	350 (28.3)	70.8 (64.1–78.3)		58.0 (53.5–62.2)	
Education levels			0.001		0.005
<High school	366 (17.1)	65.4 (58.6–73.0)		62.2 (57.4–67.4)	
High school	345 (27.2)	73.0 (62.8–83.9)		65.4 (56.8–75.9)	
>High school	645 (55.6)	55.7 (52.5–59.7)		53.0 (48.9–57.4)	
Annual household income (USD)			0.001		0.244
<25,000	420 (22.2)	65.4 (59.7–71.5)		58.0 (51.9–64.1)	
25,000–55,000	460 (32.3)	64.1 (59.7–68.7)		59.7 (53.5–66.7)	
>55,000	476 (45.5)	58.6 (53.0–64.1)		56.3 (53.0–60.3)	
BMI			0.040		0.888
<25 kg/m²	418 (33.4)	68.7 (62.2–75.9)		58.0 (53.0–63.4)	
25–30 kg/m²	490 (35.1)	59.2 (53.5–65.4)		56.3 (49.4–64.7)	
≥30 kg/m²	446 (31.4)	57.4 (53.0–62.8)		58.6 (55.2–62.2)	

Data are weighted geometric means (range) unless indicated otherwise. *Model adjusted for age, sex, and race.

ables with significant deviation from a normal distribution before further analyses.

We performed three sets of sensitivity analyses to test the robustness of our findings. First, to explore whether the associations between certain serum markers and HbAA and HbGA might be mediated by different foods (e.g., greater consumption of high-fat, high-calorie foods might result in high HbAA and HbGA and insulin resistance), we examined the associations after including daily nutrient intake (daily calories, carbohydrate, total fat, cholesterol, and fiber) from NHANES dietary interview data (23). Second, because medications such as antihyperglycemic, antihyper-tensive, and antihyperlipidemic agents might confound associations between HbAA concentrations and other glucose homeostatic markers, we performed our analyses again, including data on self-reported current medication usage. Third, because smoking is a major source of acrylamide exposure, we adjusted the smoking status both by questionnaire data and serum cotinine levels to avoid possible recall bias.

Sampling weights that account for unequal probabilities of selection, over-sampling, and nonresponse were applied for all analyses using the Complex Sample Survey module of SPSS (version 13.0 for Windows XP; SPSS, Chicago, IL).

RESULTS — The study sample included 1,356 participants (Table 1). The weighted geometric mean HbAA concentrations were adjusted for age, sex, and race/ethnicity. As shown in Table 1, the mean HbAA concentrations were higher in young adults, men, active smokers, and subjects with a lower education level, lower annual household income, and lower BMI. Weighted mean HbGA concentrations were higher in young adults, active smokers, and subjects with a lower education level. The mean ± SE values for plasma glucose, serum insulin, and HOMA-IR were 5.61 ± 0.05 mmol/l, 64.7 ± 2.9 pmol/l, and 2.89 ± 0.13, respectively. The linear associations between the

Table 2—*Linear regression coefficients with 1-unit increase in log acrylamide adducts in sample subjects*

	Model 1	P	Model 2	P
Glucose homeostasis*				
Glucose	−0.13 (0.08)	0.144	−0.09 (0.08)	0.262
Log A1C	0.00 (0.01)	0.626	0.01 (0.01)	0.253
Log insulin	−0.19 (0.06)	0.004	−0.20 (0.05)	0.001
Log HOMA-IR	−0.21 (0.06)	0.005	−0.23 (0.05)	<0.001
Lipids*				
Cholesterol	0.04 (0.07)	0.620	0.02 (0.08)	0.839
HDL cholesterol	−0.02 (0.03)	0.391	−0.05 (0.03)	0.072
Log triglycerides	−0.02 (0.04)	0.517	−0.01 (0.03)	0.742
Log C-reactive protein*	−0.10 (0.08)	0.228	−0.12 (0.12)	0.350
Waist circumference†	−2.44 (1.13)	0.047	0.44 (1.11)	0.697

Data are β coefficients (SEM). *Model 1 was adjusted for age, sex, and race/ethnicity; model 2 was adjusted for age, sex, race/ethnicity, smoking status, alcohol intake, education level, and household income, BMI, A1C, and insulin/glucose/HOMA. †BMI was not adjusted for in model 2.

HbAA levels and markers of glucose homeostasis in sample subjects are shown in Table 2. A 1-unit increase in log HbAA was associated with a decrease in the serum insulin (β coefficient = −0.20 ± 0.05, P = 0.001) and HOMA-IR (β coefficient = −0.23 ± 0.05, P < 0.001). R^2 values in the regression models were 0.363 and 0.418, respectively. The five most important determinants of serum insulin (partial R^2) were BMI (0.231), acrylamide (0.013), smoking status (0.010), age (0.007), and alcohol intake (0.006). For HOMA-IR, the five most important determinants were BMI (0.198), A1C (0.074), acrylamide (0.013), smoking status (0.009), and age (0.008). HbAA levels were not associated with plasma glucose concentrations, A1C levels, lipid metabolism, C-reactive protein levels, and waist circumference. The results were similar after subjects with diabetes were excluded (data not shown). There were no associations between HbGA levels and any of the measured parameters (data not shown).

Linear regression coefficients (SEM) between HbAA, serum insulin, and HOMA-IR levels in different subgroups of subjects are shown in Table 3. The associations between HbAA and HOMA-IR were all significant in each age-group, whereas the insulin levels were not significant in older age (≥60 years). Moreover, the HbAA levels were associated with HOMA-IR and insulin levels in each sex but were more significant in subjects who were white, ever smokers, or had a lower education level or a BMI <25 or ≥30 kg/m². We divided the HbAA levels into quartiles in the fully adjusted models, and the adjusted serum insulin levels and

HOMA-IR are shown in Fig. 1. The trends of the serum insulin levels and HOMA-IR across quartiles of the HbAA levels were significant (P < 0.001 for both).

For sensitivity analyses, we first included daily nutrient intake (log-transformed daily calories, carbohydrate, total fat, cholesterol, and fiber) in our

models. The inverse associations between HbAA concentrations and serum insulin (β coefficient = −0.25 ± 0.05, P < 0.001) and HOMA-IR (β coefficient = −0.27 ± 0.06, P = 0.001) remained significant in ever smokers. Second, after adjustment for medication usage (antihyperlipidemic, antihyperglycemic, and antihypertensive agents), the HbAA concentrations remained significantly associated with serum insulin levels (β coefficient = −0.24 ± 0.05, P < 0.001) and HOMA-IR (β coefficient = −0.26 ± 0.05, P < 0.001). Finally, the results were similar whether smoking status was obtained by questionnaire or by serum cotinine levels (data not shown).

CONCLUSIONS — Although there are several studies on the relationship between acrylamide exposure and health outcome, the relationship of acrylamide levels to diseases and laboratory abnormalities in a representative sample from a national population has never been explored. In the present study, we first showed that increased HbAA was associ-

Table 3—*Linear regression coefficients between acrylamide adducts, plasma insulin, and HOMA-IR in different subgroups*

	n	Log HOMA-IR*	P	Log insulin*	P
Age					
20–39 years	494	−0.23 (0.10)	0.038	−0.20 (0.09)	0.049
40–59 years	401	−0.22 (0.05)	<0.001	−0.22 (0.03)	<0.001
≥60 years	461	−0.25 (0.08)	0.006	−0.17 (0.10)	0.100
Sex					
Men	660	−0.20 (0.07)	0.010	−0.19 (0.06)	0.008
Women	696	−0.29 (0.07)	0.001	−0.24 (0.06)	0.002
Race					
White	732	−0.28 (0.05)	<0.001	−0.24 (0.04)	<0.001
Others	624	−0.12 (0.11)	0.273	−0.11 (0.11)	0.334
Smoking					
Nonsmoker	888	−0.19 (0.09)	0.053	−0.14 (0.09)	0.143
Ever smoker	468	−0.16 (0.04)	0.002	−0.15 (0.04)	0.002
Cotinine					
<0.1 ng/ml	736	−0.15 (0.11)	0.183	−0.08 (0.11)	0.469
≥0.1 ng/ml	620	−0.16 (0.04)	0.002	−0.14 (0.04)	0.003
Alcohol drinking status					
<12 drinks/year	681	−0.26 (0.07)	0.001	−0.23 (0.07)	0.004
≥12 drinks/year	675	−0.22 (0.07)	0.004	−0.20 (0.06)	0.006
Education levels					
≤ High school	711	−0.31 (0.07)	0.001	−0.29 (0.07)	0.001
High school	645	−0.14 (0.06)	0.025	−0.11 (0.05)	0.058
BMI					
<25 kg/m²	418	−0.29 (0.09)	0.004	−0.21 (0.09)	0.025
25–30 kg/m²	490	−0.12 (0.09)	0.165	−0.09 (0.08)	0.281
≥30 kg/m²	446	−0.33 (0.09)	0.003	−0.34 (0.09)	0.001

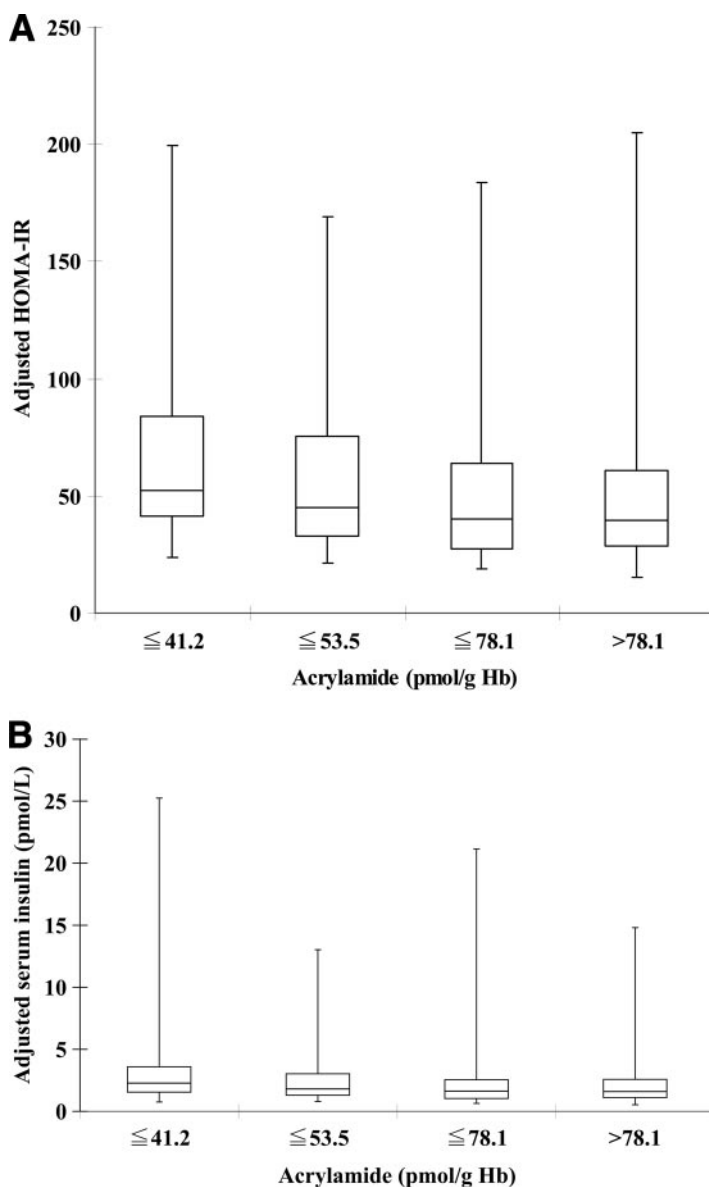Data are β coefficients (SEM). *Adjusted for the full model.

Figure 1—*Box and whisker plots of HOMA-IR* (A) *and adjusted serum insulin levels* (B) *across quartiles of the HbAA adducts in the fully adjusted model (age, sex, race, smoking status, alcohol intake, education level, household income, BMI, and plasma glucose or serum insulin). The trends of plasma insulin levels and HOMA-IR across quartiles of HbAA adducts were significant* (P < *0.001 for both).*

ated with a decrease in blood insulin and insulin resistance status in adults.

There has been a great deal of progress in the last few years in understanding the toxicology and distribution of acrylamide in animals and in humans. However, the effects of acrylamide on glucose homeostasis and lipid metabolism were addressed in only one animal study (13). In that study, male Wistar rats were fed with acrylamide, formed from frying oil heated for 20 h at 180°C, for 12 weeks. The amount of acrylamide ingested was estimated to be similar to daily human intake (0.28 ppm). All of the rats grew well, and no gross abnormalities attributable to the experimental oil were observed, except that the acrylamide-fed rats had significantly lower insulin and triglyceride levels. These findings are in accord with ours, but the causal biochemical mechanisms are not clear. Because chronic smoking is associated with insulin resistance and high insulin levels (24), it is interesting that acrylamide in cigarette smoke might counterbalance the effect of smoking on glucose homeostasis. From subgroup analyses in the present study, increased acrylamide concentrations were generally associated with de-

creased serum insulin levels, particularly in subjects who were active smokers and had a low education level and high BMI, all of which are associated with high insulin resistance. Perhaps the association between acrylamide and insulin is more obvious in subjects with high acrylamide or high insulin resistance.

In a recent animal study, rats treated with acrylamide at doses of 5.0 mg·kg^{-1}·day^{-1}) showed measurable decrements of food-motivated behavior when tested at 6–12 weeks of age. The lack of a body weight difference between treatment groups in these animals during the course of testing suggests that acrylamide may be capable of producing a direct effect on appetitive motivation in rats (14). However, the dosage used was far higher than exposure of the general human population. According to a recent cross-sectional epidemiology study in Europe, HbAA is inversely associated with BMI in smokers without adjustment for potential confounders (15). In our study, we also showed that HbAA is inversely associated with BMI and waist circumference with simple adjustment. However, after adjustment for smoking status, the association was not significant. Because smoking is an important source of acrylamide exposure and smoking could lead to weight loss, the association is probably confounded by smoking status.

Nutritional status, particularly amino acid balance, has an important effect on glutathione homeostasis (25), which may be relevant in detoxification. The adequate provision of sulfur-containing amino acids as well as glutamate and glycine is critical for the maximization of glutathione synthesis. Although there was no information about amino acid intake, the daily caloric and protein intakes were estimated to be 2,307.0 ± 44.1 kcal and 1.09 ± 0.03 g/kg, respectively, which are unlikely to lead to glutathione deficiency and therefore have little or no effect on acrylamide conjugation.

Measurements of HbAA and HbGA are expensive and difficult but well established. The modified Edman reaction method used in NHANES was successfully applied to adducts produced by acrylamide and glycidamide. This optimized method has been refined and modified in-house to increase sensitivity and enable automation. It has been widely used in several studies (8,21) and makes measurement of acrylamide exposure possible in population studies.

Our study has several limitations. First, the cross-sectional design does not permit any causal inferences. Second, exposure to acrylamide also might be an indicator of exposure to multiple chemicals, including other endocrine disruptors in smokers. If the associations reported here are confirmed in independent studies, more work will be needed to identify the mechanisms of action linking long-term, low-dose acrylamide exposure to health outcomes in humans.

In summary, we present the first report that acrylamide exposure is associated with both reduced blood insulin and insulin resistance. Because exposure to acrylamide in foodstuffs and smoking has become a worldwide concern, further longitudinal clinical and in vitro studies are urgently needed to elucidate the putative causal relationship.

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