$M+ -COOH$, $M+ -C_4H_9$, CO_2+, C_3H_7+, and C_4H_9+, respectively. This pattern suggested that R-1 was leucine. Comparison of R-1 with an authentic sample of L-leucine showed they were identical in respect to mass and infrared spectra and paper chromatography. The commercially available pure sample of L-leucine showed similar neuroactivity at $10^{-6}M$ as shown in Fig. 1b. With both R-1 and L-leucine, the highest activity appeared about 10 minutes after treatment. Thus, the neuroactive substance isolated from the blood of silkworms prostrated with DDT was identified as L-leucine. This is the first evidence for the neuroactivity of L-leucine in insects.

Substance R-3 was identified as tyrosine by paper chromatography and spectrometry. Substance R-2 could not be isolated but was presumed to be isoleucine from its R_F value. Neither the authentic sample of L-tyrosine nor that of L-isoleucine showed the neuroactivity.

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Ethnic Differences in Alcohol Sensitivity

Abstract. *Japanese, Taiwanese, and Koreans, after drinking amounts of alcohol that have no detectable effect on Caucasoids, respond with a marked facial flushing and mild to moderate symptoms of intoxication. Group differences are present at birth, and are probably related to variations in autonomic reactivity.*

The lower incidence of alcoholism among certain Mongoloid as compared to that in Caucasoid (*1*) groups is generally attributed to social-environmental factors. Although biological variations in alcohol sensitivity have been implicated in principle, no satisfactory evidence supports the claim that they contribute to the etiology of alcoholism (*2*). More generally, many anthropologists assume that population differences in behavior are determined almost entirely by cultural variables, and that the genetic contribution to differences in brain function and behavior among mating groups is at best trivial (*3*). An empirical demonstration of variations in physiological responses across ethnic groups would therefore be of theoretical interest, particularly if such variations had direct implications for psychological adaptation.

Having observed that many Mongoloids respond with a rapid intense flushing of the face annd with symptoms of mild to moderate intoxication after drinking alcohol in amounts that have no apparent effect on Caucasoids (*4*), I systematically compared the alcohol flushing responses of Caucasoid and various Mongoloid groups. The subjects were randomly selected, healthy Caucasoid and Mongoloid men and women between 25 and 35 years old, residing in the United States, Japan, Taiwan, and Korea, respectively. To control for cultural differences in alcohol consumption, diet, and other postnatal environmental influences, I also compared the flushing responses of healthy full-term Caucasoid infants with those of Japanese and Taiwanese infants.

Flushing was determined by optical densitometry of the earlobe and inspection of the face (*5*). Since the densitometer response was linear in the range of values tested, differences in baseline optical density due to variations in skin pigmentation probably did not affect the results.

Subjects were tested at least 2 hours after a meal. Room temperature was always maintained at a comfortable level. All adults drank beer (5 percent alcohol by volume); and Caucasoids received consistently more alcohol per unit of body weight (0.36 to 0.45 ml/kg) than Mongoloids (0.14 to 0.30 ml/kg) (*6*). During the test subjects were asked to report any subjective symptoms that might be related to drinking; afterward they filled out a short questionnaire about their weekly consumptions of alcohol, their predisposition to intoxication, and the incidence of flushing in their families. Infants were tested by giving them small amounts of port wine in 5 percent glucose solution; no side reactions were produced. Caucasoid infants again received consistently more alcohol per body weight (0.34 to 0.45 ml/kg) than Mongoloid infants (0.16 to 0.23 ml/kg).

The results indicate that 83 percent of Mongoloid adults responded with a marked visible flush and an increase of optical density greater than 5 mm (mean increase 34.3 mm; range 14 to 78 mm), whereas only 2 of the 34 Caucasoid adults (6 percent) showed any increase of optical density greater than 5 mm, and only 1 of these flushed visibly. Population differences in flushing response were statistically significant ($P < .001$; see also Table 1). Ten nonreacting Caucasoids who subsequently

Table 1. Flushing responses, and increases of optical density and pulse pressure in the earlobe, after ingestion of alcohol. In each case, the Caucasoid population is compared to a corresponding Mongoloid group. Since only records free of artifacts were tabulated, whereas mean changes of optical density were calculated for the entire subgroup, the magnitude of flushing responses among Korean subjects appears to be less than that among other Mongoloid subgroups. This conclusion is not warranted by the results.

Group	Sample size (No.)	Visible flushing (No.)	Optical density		Pulse pressure	
			Increase > 5 mm (No.)	Mean increase for total (mm)	Measurable increase (No.)	Mean increase for total (%)
Caucasoid						
Adults	34	1	2	1.1	1 (?)	5 (?)
Infants	20	1	1	1.7	0	
Japanese						
Adults	38	32*	34*	36.8†	33*	257†
Infants	25	17*	17*	16.8†	9	
Taiwanese						
Adults	24	19*	20*	37.7†	19*	246†
Infants	10	9*	9*	14.6†	4	
Korean						
Adults	20	14*	10*‡	17.4†‡	9*‡	161†

* Ethnic group differences are significant at $P < .001$, chi-square test. † $P < .001$, *t*-test. ‡The records of six Korean subjects could not be analyzed reliably because of line-voltage disturbances.

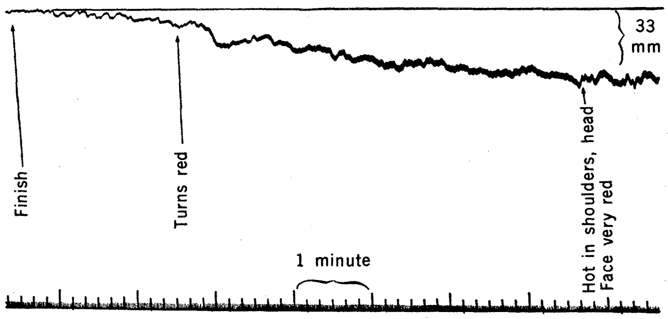

Fig. 1. Increase of optical density of the earlobe and pulse pressure in earlobe after alcohol ingestion, in a Japanese adult male. Optical density begins to change 2 minutes after completion of drinking; after 8 minutes, optical density has increased 33 mm. Changes in pulse pressure are indicated by an increase in thickness of the channel registering optical density. Actual changes of pulse pressure are calculated from records made at a faster paper speed in order to show individual pulses.

drank larger amounts of alcohol (0.54 to 0.60 ml of alcohol per kilogram of body weight), showed neither a visible flush nor an increase in optical density, although seven of the ten reported mild symptoms of intoxication.

Optical density began to increase 2 to 7 minutes after the completion of drinking, and reached a peak at 30 to 37 minutes. These latencies in response correspond closely to the time when alcohol in the blood can first be detected and when the amounts in the blood reach a peak in Caucasoid adults who had ingested one moderate dose of alcohol on an empty stomach (*7*). Group differences in alcohol absorption, therefore, probably did not contribute to the observed differences. The short period of latency between drinking and onset of flushing also suggests that the higher incidence of flushing in Mongoloids was not due to their slower alcohol metabolism (*8, 9*).

The densitometer recorded moment to moment changes of pulse pressure as phasic excursions of the recording pen, which, as shown by electrocardiogram, were correlated directly with heartbeat. A strong flush was almost always associated with an increase of 100 to 350 percent in the width of pen excursions (or relative increase of pulse pressure), and reached a peak at about the same time that flushing was most apparent, and at the time when strong reactors reported a pounding sensation in their heads. Relative increases of pulse pressure were observed in 74 percent of Mongoloid adults and in only one Caucasoid (3 percent) Table 1 and Fig. 1).

Table 2. Subjective symptoms after alcohol consumption in Caucasoid and Mongoloid adults.

Symptom	Group			
	Caucasoid ($N = 34$)		Mongoloid ($N = 78$)	
	%	No.	%	No.
Hot in stomach	5.8	2	52.5*	41
Palpitations	0		25.7*	20
Tachycardia	2.9	1	43.5*	34
Muscle weakness	2.9	1	25.7†	20
Dizzy	8.6	3	37.2†	24
Sleepy	5.8	2	33.4†	26
Falls asleep	0		18.0†	4

$^*P < .001$. $^†P < .01$.

Population differences with respect to flushing after alcohol consumption were as clear-cut among infants as adults. Of all Mongoloid infants tested, 74 percent responded with a visible flush and an increase of optical density greater than 5 mm. In contrast only 1 of the 20 Caucasoids showed a visible flush and a measurable densitometer response (Table 1). The differences were statistically significant ($P < .001$). Changes of pulse pressure could not be measured reliably in infants, but were noted to occur in one-third of those who flushed visibly. Since newborn infants showed the same group-dependent variations in alcohol response as adults, postnatal dietary factors and cultural variations in drinking habit did not account for the observed differences.

The incidence of flushing among adult subjects was paralleled by a similar distribution among their parents. Of Mongoloid adults tested, 94 percent reported that at least one of their parents flushed consistently after drinking, whereas only 1 of the 34 Caucasoids had ever noted that either of his parents flushed as a result of consuming alcohol. Mongoloids also reported significantly more symptoms of intoxication than Caucasoids (Table 2). The greater alcohol sensitivity of Mongoloids was therefore not limited to vasodilatation of the facial vessels, but extended to other physiological systems and particularly those under autonomic nervous system control.

Whether these findings are related to the etiology of alcoholism is open to question. The vascular response to drinking and the associated subjective symptoms of intoxication experienced by Mongoloids may well prevent many of them from consuming even moderate quantities of alcohol.

Cutaneous vasodilatation after alcohol ingestion is probably the result of central vasomotor depression (*8, 10*). By extrapolation, population differences in flushing to alcohol may be assumed to reflect a specific and probably genetic difference in autonomic nervous system responsivity that is common to all of the tested populations belonging to the "Mongoloid major group" (*3, 11*). The assumption that ethnic group differences in autonomic regulation have a genetic basis is compatible with other reports of racial differences in autonomic responses to selected pharmacologic agents (*4, 12*).

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References and Notes

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