Relationships among Panic-Fear Personality, Aging, and Ventilatory Activity

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Tanaka, Y., Nishibayashi, Y., Maruyama, R., Morikawa, T. and Honda, Y. *Relationships among Panic-Fear Personality, Aging, and Ventilatory Activity.* Tohoku J. Exp. Med., 1988, 156, Suppl., 189-199 —— We have studied 204 healthy male subjects ranging in age from 20 to 59 years. They were divided into four 10-year age groups. Each age group was further divided into 2 subgroups with high and low Panic-Fear scores. The ventilatory activities of all the groups were compared. In the younger generation (20-39 years), the low PF group revealed a higher slope in CO_2 response curve than the high PF group ($p < 0.05$). This result was considered to be related to the difference in CO_2 production between the two groups. In the older age groups, however, the high PF subjects exhibited a tendency to increase the CO_2 response slope with increasing ages. This contradictory result was thought to be due to the age dependent change in biogenic amine activity. —— personality; Panic-Fear scale; aging; CO_2 response; biogenic amines

A number of physiological and pathophysiological factors are known to affect breathing in man, i.e., age, sex, body size, sports activities, high altitude and certain kinds of diseases to name a few (Patric and Howard 1972; Kawakami et al. 1981). Therefore, care must be taken in assessing the data to see if any of these factors may have led to some deviation in the experimental conditions. Recently, a few investigators proposed that personality has some influence over the ventilatory responses (Clark and Cochrane 1970; Saunders et al. 1972; Arkinstall et al. 1974; Hudgel and Kinsman 1983). Their findings seemed to generally agree on the fact that the more extraversive personality shows higher ventilatory responses than the personality which tends to be more introverted (Clark and Cochrane 1970; Saunders et al. 1972; Arkinstall et al. 1974), and also that irritability correlates with ventilatory depression (Clark and Cochrane 1970; Hudgel and Kinsman 1983). The former finding also appears reasonable to us, but the latter may be more difficult to agree with readily. For this reason we

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conducted a preliminary study and noticed that such an "irritable" personality may be correlated not only with ventilatory activity but also with metabolic activity. The present study was then undertaken to confirm this observation, and the possible underlying mechanisms were considered in detail.

METHOD

We studied 237 factory workers ranging in age rom 20 to 59 years, and 204 of them, judged free of any diseases, were used for further analysis. All subjects were male. They were not familiar with the experimental procedure of using a mouthpiece and noseclip. Each subject was kept free of food and caffeine intake for at least 2 hr prior to the experimental procedure. Since the majority of subjects are usually engaged in physical labour, they were requested to refrain from such hard work as much as possible on the experimental day.

The experiments were performed in a quiet area in the health facilities of the factory. Each subject was asked to rest for about 30 min before the examination. During this period they were informed about the test procedures, and filled in the Panic-Fear score sheet, considered to be the most reliable method for estimating mental irritability (Dirks et al. 1977; Hudgel and Kinsman 1983). Then, each subject sat on chair and breathed through a mouthpiece connected to a one-way valve. Between the mouthpiece and one-way valve, a hot wire flowmeter (RF-H, Minato, Tokyo) was inserted for detecting the breath by breath respiratory flow. Tidal volume (V_T), inspiratory duration (T_I), and expiratory duration (T_E) were computed electronically using a home-made integrator. End-tidal PCO_2 and PO_2 ($P_{ET}CO_2$ and $P_{ET}O_2$) were simultaneously measured using a rapid response O_2 and CO_2 analyzer (1H21, San-ei, Tokyo). Expired air was introduced into a smoothing bag connected to the outlet of the experimental setup. When the ventilatory pattern of each subject achieved a steady state condition, the sampling line of the O_2 and CO_2 analyzer was moved to the outlet of the smoothing bag, and expiratory PCO_2 and PO_2 (P_ECO_2 and P_EO_2) were determined. After these measurements, hypercapnic ventilatory response (HCVR) was examined with Read's rebreathing method. Each rebreathing run was continued untill $P_{ET}CO_2$ reached around 65 mmHg.

The Panic-Fear score sheet consists of 15 questions. Each subject answered in a yes/ no manner, and he was scored by the absolute number of scoreable answers (Dirks et al. 1977).

Using the data obtained from the ventilatory variables at rest, minute ventilation ($\dot{V}_E$), breathing rate (f), O_2 consumption ($\dot{V}O_2$), and CO_2 production ($\dot{V}CO_2$) were calculated. Then, the slope of the metabolic hyperbola (S_L) at resting $P_{ET}CO_2$ in each trial was calculated by the equation:

$$-0.863 \cdot \dot{V}CO_2/(P_{ET}CO_2)^2 \text{ (Honda et al. 1983)}.$$

The HCVR line was expressed by linear line regression between $P_{ET}CO_2$ and $\dot{V}_E$ or $P_{ET}CO_2$ and alveolar minute ventilation ($\dot{V}_A$) during CO_2 rebreathing.

$$\dot{V}_E = S (P_{ET}CO_2 - B), \text{ or}$$
$$\dot{V}_A = S_A (P_{ET}CO_2 - B_A)$$

where S and S_A, and B and B_A are the slope and the horizontal intercepts of the regression lines, respectively. The overall "gain" (G or G_A), defined by the ratio of S or S_A to S_L, was also calculated (Honda et al. 1983). Here to determine $\dot{V}_A$, we assumed a constant respiratory dead space (V_D), which was calculated from the data at rest using the following equation:

$$V_D = (P_{ET}CO_2 - P_ECO_2) \cdot V_T/P_{ET}CO_2.$$

The behavioral influence of holding the mouthpiece during the rest (Gardner 1977;

Hirsch and Bishop 1982) was evaluated by the amount of $P_{ET}CO_2$ depression ($\Delta P_{ET}CO_2$) as follows: After holding the mouthpiece in place, averaged $P_{ET}CO_2$ of the first breaths was obtained, and then this value was subtracted from $P_{ET}CO_2$ at rest.

The data analysis was conducted as follows: Our subjects were classified into four 10-year age groups: 20–29, 30–39, 40–49, and 50–59 years old. Each age group was subdivided into two groups according to the PF score, i.e., 0–4 as the low and 5 and higher as the high score group. This classification was based on the mean PF score of all the subjects; 4.24. Statistical analysis was performed between the two subgroups of each age group, as well as of all the subjects in relation to the various age groups, using the Student's t-test. The distribution of the data was also examined by the use of the "F" test.

RESULTS

Profile of the subjects. Since our subjects were randomly selected, the number belonging to each age group was not uniform, affected by the ununiform constriction of generation belonging to the company (Fig. 1). The greatest number was in the highforties, and become less with younger subject groups, although even the smallest group still consisted of as many as 29 subjects.

The PF scores of the subjects ranged from 1 to 10, with a mean score of 4.24 (Fig. 2). However, as is shown in Fig. 1, their distribution among all the age group was not uniform. The tendency was that the higher the age, the higher the PF score. Body surface area (BSA) was apparently larger in those in their twenties than in the other age groups ($p < 0.01$), and this difference between the high and low PF groups in the twenties' group was also significant ($p < 0.05$)
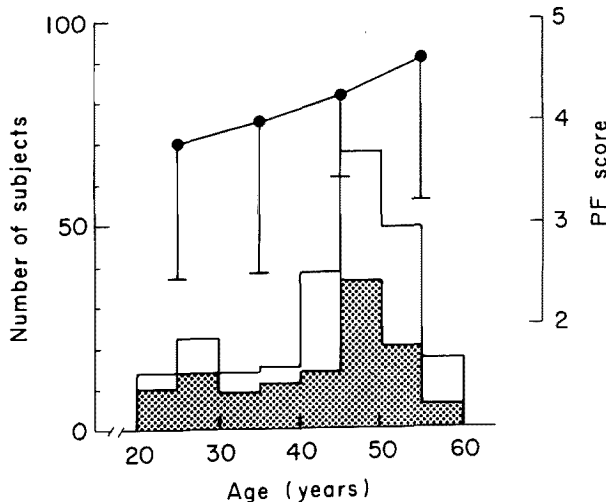

Fig. 1. Distribution of number of subjects shown by histogram of 5-year groups. The open column represents the number of high Panic-Fear (5–15) subjects, whereas the crosshatched column the low PF (0–4) subjects. Continuous line connecting closed circles reveals the tendency that PF score (mean ± S.E. of each 10 year group) increases with increasing age.
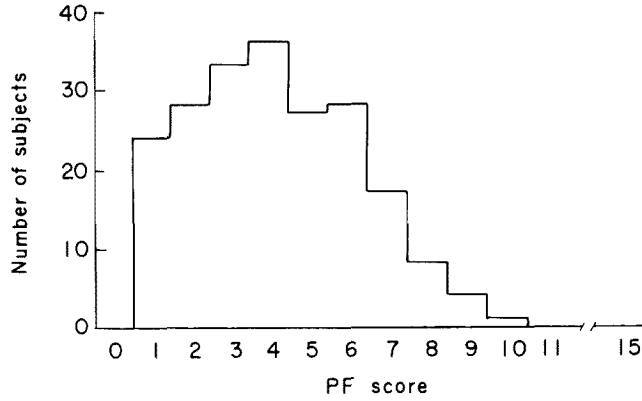
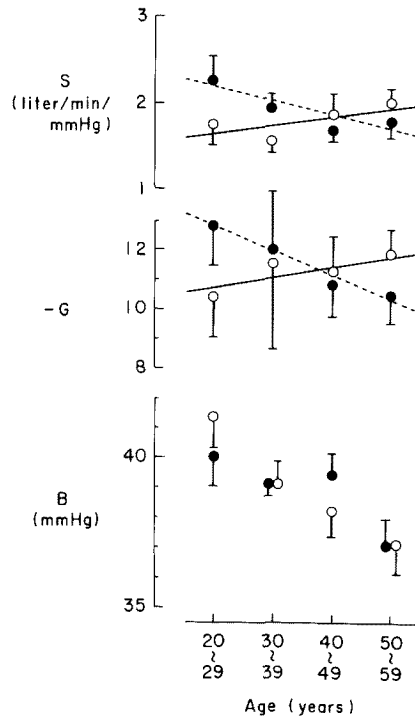Fig. 2.   Distribution of PF scores in a histogram.

Fig. 3.   Slope of CO_2 response curve (S), intercept of response line on abscissa (B),
and overall "gain" of the ventilatory controlling system (G) in 20's to 50's
subject groups.   ● : mean value of each parameter of subjects with low PF
scores (0-4).   ○ : mean value of each parameter of subjects with high PF
scores (5-15).   Vertical line represents SE of each mean.   Continuous and
broken lines were drawn by eye, taking into consideration the weighted mean
of each subject group.

TABLE 1. *Ventilation pattern, influence of mouthpiece breathing, and metabolic parameters*

		Age (years)							
		20–29		30–39		40–49		50–59	
		PF score classification							
		L(24)	H(12)	L(20)	H(9)	L(50)	H(40)	L(26)	H(23)
$\dot{V}_E$	(liter/min)	10.33±2.67	9.98±2.83	9.66±1.59	9.15±2.38	9.12±1.70	9.81±1.92	9.91±2.57	10.13±3.32
V_T	(ml)	750±180	750±310	610±130	750±190	650±180	680±170	650±180	620±70
f	(breath/min)	14.6±5.4	15.9±9.0	16.5±5.0	13.2±5.7	15.0±4.8	15.6±5.6	16.2±5.8	16.9±7.9
$P_{ET}CO_2$ at rest	(mmHg)	38.3±2.4	37.3±2.1	38.6±1.9	37.8±2.1	38.3±2.7	37.7±2.3	36.4±2.9	37.5±1.9
$\Delta P_{ET}CO_2$	(mmHg)	−0.3±3.0	−0.8±1.1	−1.6±2.6	−3.3±4.3	−1.4±3.1	−2.2±3.2	−1.7±2.2	−2.7±4.3
$\dot{V}CO_2$	(ml/min)	304±55	288±57	271±48	269±39	264±58	279±55	272±59	263±33
$\dot{V}O_2$	(ml/min)	394±76	364±90	323±41	300±50	319±50	330±55	312±58	311±50
BSA	(m²)	1.88±0.13	1.78±0.15	1.77±0.13	1.78±0.06	1.72±0.10	1.71±0.10	1.67±0.07	1.69±0.08

Values are means±s.d. Numbers in parentheses are the numbers of subjects.
PF, Panic-Fear; L and H, low and high PF score subjects, respectively; $\Delta P_{ET}CO_2$, magnitude of $P_{ET}CO_2$ depression due to mouthpiece breathing.

TABLE 2. *Parameters of CO_2 controlling system and metabolic hyperbola*

		Age (years)							
		20–29		30–39		40–49		50–59	
		PF score classification							
		L(24)	H(12)	L(20)	H(9)	L(50)	H(40)	L(26)	H(23)
−G	(liter/min/mmHg)	12.84±6.61	10.47±4.83	12.00±4.00	11.60±8.80	10.87±7.32	11.28±7.58	10.47±4.60	11.89±3.66
S	(liter/min/mmHg)	2.24±0.97	1.74±0.58	1.94±0.72	1.56±0.32	1.70±0.94	1.85±1.18	1.81±0.87	2.00±0.67
B	(mmHg)	40.0±4.9	41.3±3.6	40.1±2.1	39.1±2.3	39.5±4.2	38.2±5.4	37.1±4.6	37.2±5.0
−G_A	(liter/min/mmHg)	10.37±5.94	9.61±4.66	10.23±3.98	9.07±7.31	9.60±6.36	9.63±6.93	8.67±4.32	9.50±5.00
S_A	(liter/min/mmHg)	1.99±0.86	1.60±0.54	1.76±0.68	1.70±0.61	1.55±0.82	1.75±1.14	1.69±0.84	1.87±0.74
B_A	(mmHg)	42.6±4.6	42.6±4.1	43.0±3.9	41.2±2.3	41.7±4.2	41.4±4.4	40.0±4.9	40.0±4.7
−S_L	(liter/min/mmHg)	0.18±0.03	0.18±0.05	0.16±0.03	0.17±0.05	0.16±0.04	0.17±0.04	0.18±0.07	0.16±0.03

Values are means±s.d. Number in parentheses is the number of subjects.
−G, overall loop-gain of the CO_2-$\dot{V}_E$ feedback control system; S and B, slope and horizontal intercept of CO_2-$\dot{V}_E$ response curve, respectively; −G_A, overall loop-gain of the CO_2-$\dot{V}_A$ feedback control system; S_A and B_A, slope and horizontal intercept of CO_2-$\dot{V}_A$ response curve, respectively; −S_L, slope of the metabolic hyperbola.
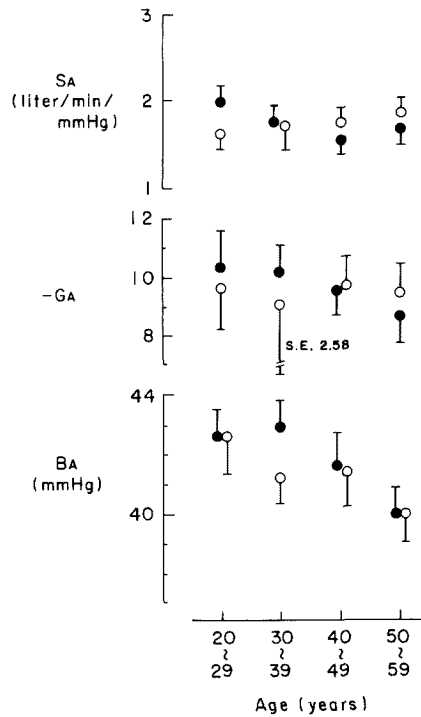
Fig. 4. Slope of $P_{ET}CO_2$-$\dot{V}_A$ response curve (S_A), intercept of response line on abscissa (B_A), and overall "gain" of the ventilatory controlling system (G_A). Symbols same as Fig. 3.

(Table 1 and Fig. 5).

Ventilatory pattern, ventilatory and metabolic activities, and influence of mouthpiece breathing. Despite significant differences in BSA, the magnitude of $\dot{V}_E$ was more or less the same among all age groups (Table 1). V_T decreased gradually with increasing age ; the differences between the youngest group and those in their fourties ($p < 0.05$) and fifties ($p < 0.01$) were significant. Despite significantly larger BSA in the low than the high PF score subgroup in the youngest group, V_T was nearly the same. Therefore, the difference in V_T among all the age groups may be related to age rather than body size. In accordance with this tendency, f gradually increased with increasing age. $P_{ET}CO_2$ at rest under mouthpiece breathing was markedly reduced in the older subjects ; the difference between the youngest and oldest groups was significant ($p < 0.05$). This fact may be partly explained by the gradual decrease in $\Delta P_{ET}CO_2$ with age. The absolute magnitude of $\Delta P_{ET}CO_2$ was significantly larger in the older age groups than the youngest ($p < 0.01$), i.e., older subjects were more sensitive to the mouthpiece and tended to overventilate under this condition.

Although it was not statistically significant, $\Delta P_{ET}CO_2$ also was less in the low than in the high PF score subjects in all age groups. $\dot{V}CO_2$ was apparently higher
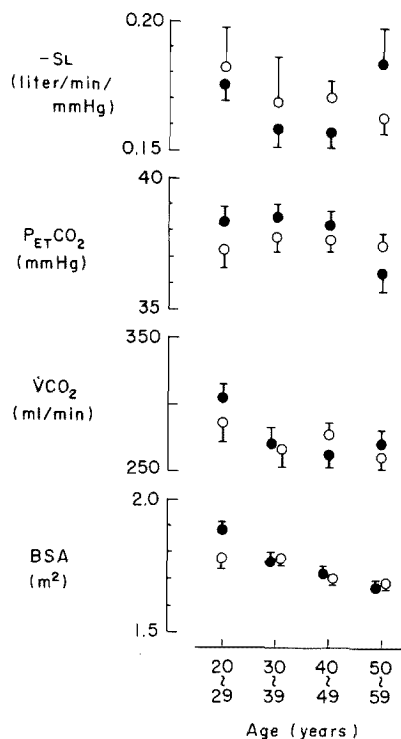
Fig. 5. Slope of metolic hyperbola (S_L), $P_{ET}CO_2$ at rest, $\dot{V}CO_2$, and BSA. Symbols same as Fig. 3.

in the youngest group than in their thirties, fourties ($p < 0.05$) and fifties ($p < 0.01$), despite the occurrence of hyperventilation in the older subjects. Similar findings were noticed in the $\dot{V}O_2$ data; the youngest group showed larger $\dot{V}O_2$ than their senior subjects ($p < 0.05$). There was no consistent difference in the metabolic rate between high and low PF score subjects, although the low PF score of the twenties' group showed a somewhat higher value. As a result of all the composite influences of these observed variables, the slope of metabolic hyperbola (S_L) under mouthpiece breathing was found to be almost the same among all the age groups and PF score groups.

Hypercapnic ventilatory responses and overall gains of the ventilatory control system. Borderline significance was seen in the CO_2-ventilation response slope (S) between the high and low PF score subjects in the youngest group. When S values in the twenty and thirty year old groups were pooled together, the mean S in the high PF subjects become significantly less than that in the low PF subjects ($p < 0.05$). However, this relationship developed a tendency to reverse itself in the older age groups. Such biphasic findings were also true in the data of S_A, although to a lesser degree.

S and S_A were then divided by S_L to obtain G and G_A, respectively. The magnitude of the overall gain showed similar features to those seen in the CO_2
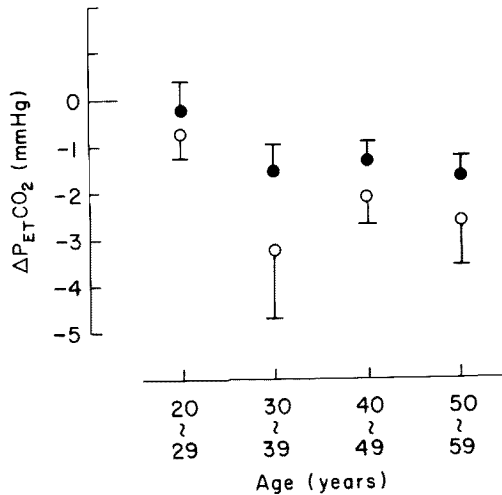
Fig. 6.   Magnitude of $P_{ET}CO_2$ depression ($\Delta P_{ET}CO_2$) by mouthpiece breathing in
each age group.   Symbols same as Fig. 3.

response slopes.   As a result of these inverse trends of the two PF score groups
with age, the aging effect on S (S_A) and G (G_A) disappeared when the personality
difference was not taken into account.   B and B_A, on the other hand, consistently
decreased with increasing age.   Significant difference was found between the
follwing age group pairs : 20-29 and 50-59 ($p < 0.01$), 30-39 and 50-59 ($p < 0.05$),
and 40-49 and 50-59 ($p < 0.05$) in B values, and 20-29 and 50-59 ($p < 0.05$), and
30-39 and 50-59 ($p < 0.05$) in B_A values, respectively (Table 2).

DISCUSSION

The Panic-Fear personality, which was first proposed by Dirks et al. (1977),
describes fearful, emotionally labile indivisuals who profess to be more sensitive
than others, and who are unable or disinclined to persist in the face of difficulty.
Although the expression of such a personality may be merely a problem of
psychology, several attempts have been made to explain such a personality
biophysiologically according to the effects of specific biogenic amines, periferally
and centrally.

Reviewing previous reports related to anxiety or fear, the following concepts
seem to be generally accepted (Schildkraut and Kety 1967 ; Murphy and Red-
mond 1975 ; Redmond 1977 ; Mueller et al. 1982) : 1) Epinephrine or norepine-
phrine administered peripherally or centrally may cause anxiety, fear, or similar
reactions in animals and human ; 2) In the face of psychological stress, the release
of catecholamines becomes enhanced in animals and human ; 3) In somekind of
manic depressive patients, urinary excretion of catecholamines is greater during
the manic than the depressed phase ; 4) Many drugs which are anxiolytic in
humans diminish the turnover rate of catecholamines.

From these findings, it seems very likely that anxiety or fear may be associated with elevated catecholamine levels at functionally active adrenergic receptors in the brain, although not all the complex phenomena may be explained exclusively by such changes in the metabolism of the biogenic amines. Accordingly, the Panic-Fear personality may possibly be related to the activated adrenergic functions in certain brain organizations. However, as we did not measure the differences in catecholamine level between high and low PF score subjects, it was not possible to either confirm or deny this presumption. However, there does appear to be a fairly consistent relationship between the pharmacological effect of these amines and the biological response against anxiety and fear. In addition, the present observation that the average PF score increases with age may give further support to this hypothesis, because it is known that the catecholamine level increases with age (Lake et al. 1976; Ziegler et al. 1976). In contrast, however, Robinson (1975) reported that central catecholamine decreases with age. Yet, because his data were obtained by autopsy, judjing from the unstable chemical properties of catecholamines (Lake et al. 1976) together with the increased monoamine oxidase activity with age (Robinson et al. 1975), it is doubtful that his finding is reliable. Furthermore, it has also been reported that according to the analysis of cerebrospinal fluid, central catecholamine rather increases with age (Gottfried et al. 1971).

The ventilatory effect of catecholamines is believed to be stimulatory (Whelan and Young 1953; Young 1957; Cunningham et al. 1963; Mueller et al. 1982; Schoene et al. 1982). Thus, if we regard the above hypothesis to be true, the higher PF score may be correlated to the higher ventilatory activity. The consistently larger $\Delta P_{ET}CO_2$ in the high PF score subjects among all age groups seems to express the higher ventilatory activity when the subjects were submitted to the experimental apparatus (Gardner 1977). The decrease in B or B_A values with age, which may suggest increased hypercapnic sensitivity in older subjects, is also explained by the possibly increased catecholamine level in the older generation. The ventilatory activities expressed by S (S_A) or G (G_A) seem to show results which are rather in conflict with this theory in the younger generation, where we noticed a larger $\dot{V}CO_2$ and S or in the low than the high PF score subjects. As has been repeatedly proposed in recent works, the major factor for determining the ventilatory activity seems to be the CO_2 production, at least in healthy subjects (White et al. 1985). Therefore, the stronger ventilatory activity of low PF subjects in the younger generation may be caused by their higher metabolic rate (Table 1, Fig. 5). In summary, we concluded that our present observations could be explained by the possible difference of catecholamine level in each age group and by the difference in metabolic activity in younger people.

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