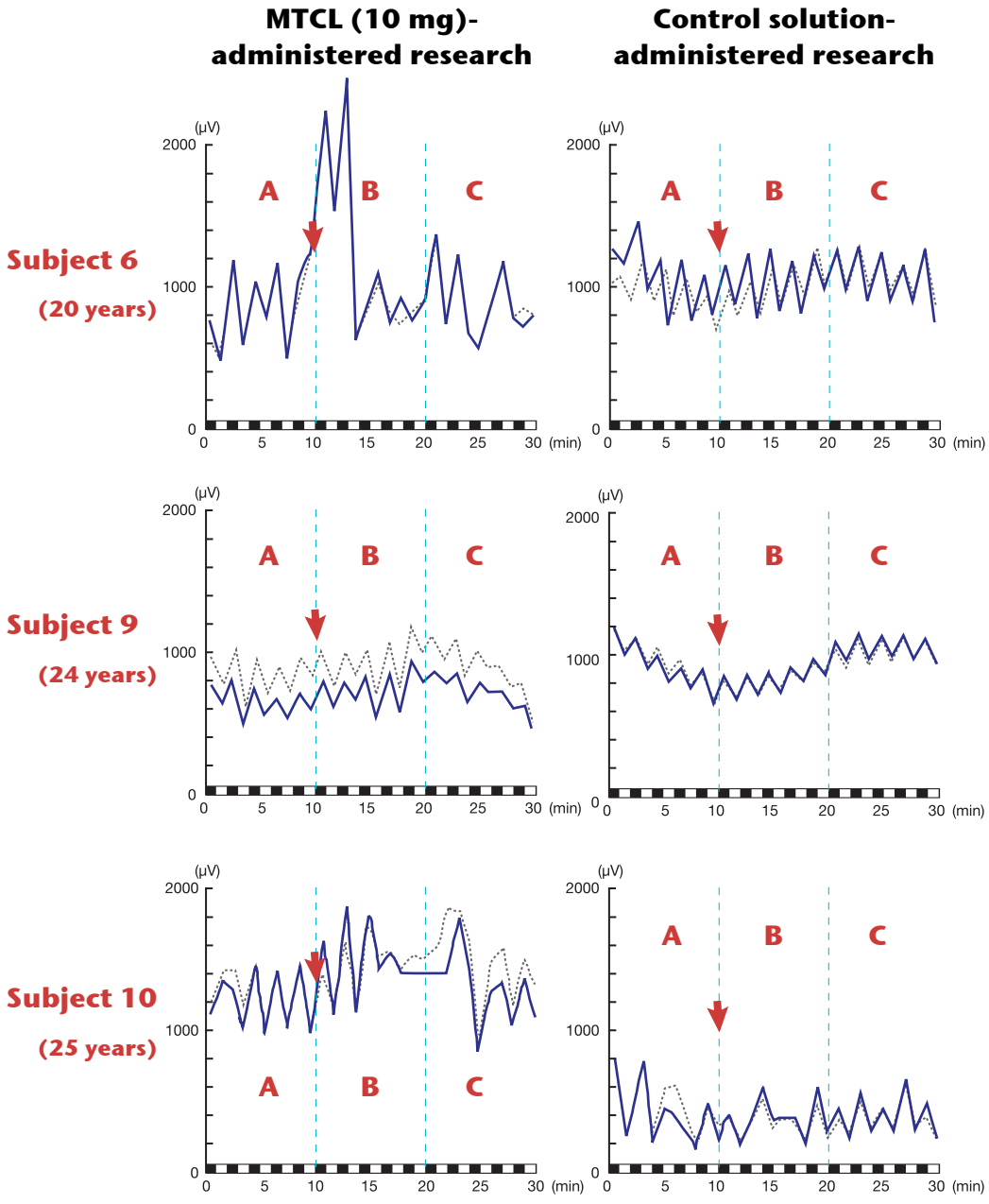

Fig. 3. Some samples of FO patterns of 5 female test subjects. The dotted line in each sample shows FO pattern in the right eye and the solid line shows that in the left eye. Control solution: physiological saline. A, phase A: initial 10 min before intravenous injection; B, phase B: following 10 min after the injection; C, phase C: additional 10 min after the injection. A dark arrow in each sample indicates the injection point. ■, dark period; □, light period (horizontal axis).

Results

Figures 2 and 3 demonstrate some samples of FO patterns obtained in the MTCL (10 mg)- and control solution-administered researches in the male and female test subjects, respectively. After administration of MTCL, markedly fluctuated FO patterns were observed in both eyes of each subject in both groups, especially in the female group in phases B and C after administration, compared with their FO patterns in phase A before administration.

Table 1. The df_{FO} results obtained in the MTCL (10 mg)- and control solution-administered researches in 10 eyes of 5 male healthy volunteers

Subject Number	Age (year)	Measured eye	MTCL (10 mg)-administered research (μV) Phase A	Phase B	Phase C	Control solution-administered research (μV) Phase A	Phase B	Phase C
1	22	Right	126.1	170.4	127.0	46.1	49.2	146.3
		Left	116.5	170.4	104.3	46.9	60.9	178.3
2	21	Right	208.4	224.0	396.0	276.4	197.0	171.2
		Left	238.8	253.5	421.0	320.6	257.4	210.8
3	23	Right	123.4	183.0	175.0	120.2	150.2	130.0
		Left	147.6	197.4	169.0	144.8	145.8	161.4
4	22	Right	173.9	172.1	213.7	178.3	158.2	211.3
		Left	165.2	181.0	228.4	218.3	175.7	193.9
5	21	Right	133.9	193.5	185.5	122.6	157.4	167.8
		Left	159.1	175.7	184.8	160.0	190.4	206.1
Mean			159.3	192.1	220.5	163.4	154.2	177.7
SD			39.4	27.0	105.7	89.4	61.6	27.8
Statistical analysis (Wilcoxon's rank sum test)			$P < 0.01$	NS		NS	NS	
			$P < 0.01$			NS		
NS, not significant ($P > 0.05$)			NS					

Control solution: physiological saline.
Phase A: initial 10 min before intravenous injection. Phase B: following 10 min after the injection. Phase C: additional 10 min after the injection.

Table 2. The dfFO results obtained in the MTCL (10 mg)- and control solution-administered researches in 10 eyes of 5 female healthy volunteers

Subject Number	Age (year)	Measured eye	MTCL (10 mg)-administered research (μV) Phase A	Phase B	Phase C	Control solution-administered research (μV) Phase A	Phase B	Phase C
6	20	Right	391.8	1235.5	539.7	308.0	269.2	314.8
		Left	453.0	1203.5	499.0	345.6	363.4	352.8
7	19	Right	60.4	79.3	100.3	28.4	79.0	86.2
		Left	64.0	61.0	79.0	36.8	58.2	88.4
8	21	Right	156.4	150.0	250.5	110.4	223.0	69.0
		Left	120.6	152.0	266.0	149.8	178.4	99.0
9	24	Right	219.2	267.6	186.2	198.0	137.6	160.8
		Left	189.6	186.2	146.2	188.2	127.8	156.4
10	25	Right	259.0	293.0	274.3	246.6	162.5	193.2
		Left	271.4	522.3	314.0	289.0	261.0	233.8
Mean			210.3	443.8	265.5	190.1	186.0	175.4
SD			130.2	415.0	154.5	109.9	94.0	98.8
Statistical analysis (Wilcoxon's rank sum test)			$P < 0.025$	NS		NS	NS	
			$P < 0.05$			NS		
NS, not significant ($P > 0.05$)			NS					

Control solution: physiological saline.
Phase A: initial 10 min before intravenous injection. Phase B: following 10 min after the injection. Phase C: additional 10 min after the injection.

Table 3. Comparison of the df_{FO} values obtained in the MTCL (10 mg)- and control solution-administered researches in the male and female groups (10 eyes of 5 healthy volunteers each)

Research	Statistical analysis†	Male group (μV)			Female group (μV)		
		Phase A	Phase B	Phase C	Phase A	Phase B	Phase C
MTCL (10 mg)-administered	Mean	159.3	192.1	220.5	210.3	443.8	265.5
	SD	39.4	27.0	105.7	130.2	415.0	154.5
		NS					
			$P < 0.05$				
				NS			
Control solution-administered	Mean	163.4	154.2	177.7	190.1	186.0	175.4
	SD	89.4	61.6	27.8	109.9	94.0	98.8
		NS					
			NS				
				NS			

† Wilcoxon's rank sum test: NS, not significant ($P > 0.05$).
Control solution: physiological saline.
Phase A: initial 10 min before intravenous injection. Phase B: following 10 min after the injection. Phase C: additional 10 min after the injection.

It is of note that a 20-year-old female (Subject 6) showed a highly fluctuated FO pattern associated with increased FO potential after administration of MTCL in phase B, though no remarkable changes were observed in her FO pattern after administration of the physiological saline control solution in phase B (Fig. 3).

Main examination

df_{FO} results obtained in the male and female groups

After administration of MTCL, the mean level of df_{FO} significantly increased between phase A and phase B in the male and female groups ($P < 0.01$ and $P < 0.025$) and between phase A and phase C in both groups ($P < 0.01$ and $P < 0.05$), though no statistically significant differences ($P > 0.05$) were detected in the mean level of df_{FO} between phase B and phase C in either the male or female group (Tables 1 and 2).

Comparison of df_{FO} values between the 2 groups

In comparing the df_{FO} values between the two groups, the mean level of df_{FO} of the 10 eyes of the 5 female test subjects was significantly higher than that of the 10 eyes of the 5 male test subjects in phase B ($P < 0.05$), though no statistically significant differences ($P > 0.05$) were detected in the mean level of df_{FO} in phase A or phase C in MTCL (10 mg)-administration (Table 3).

Control examination

The control examination using physiological saline was performed at least 2 weeks after the main examination. No statistically significant differences ($P > 0.05$) were detected in the mean levels of df_{FO} in either the male or female group in the comparison of the df_{FO} values in phase A between control solution-administration and MTCL (10 mg)-administration (Tables 1 and 2), though relatively larger fluctuations in FO potential were apparently observed in the female sample cases than in the male ones (Figs. 2 and 3).

After administration of the control solution, no statistically significant differences ($P > 0.05$) were detected in the mean level of df_{FO} in either the male or female group throughout the experiment (Tables 1 and 2), even in the comparison of the df_{FO} values between the two groups (Table 3).

Discussion

In the present study, the measuring time of 30 min was tentatively divided into 3 phases (A, B and C) of 10 min each, and the results obtained from each phase were compared with one another, to minimize the influence of SO on FO (Kolder and Brecher, 1965; Kolder, 1974; Nikara et al., 1974; De Rouck and Kayembe, 1981; Thaler et al., 1982; Welber, 1989) and to reflect on reaction time after MTCL administration (Schulze-Delrieu, 1979; Maruiwa et al., 1992).

The ratio of the osmotic pressure from Primperan injection which was adopted in the present survey is approximately 1.0 to physiological saline used as a control solution. Thus it is difficult to imagine that the osmotic pressure in the blood might influence the FO potential (Kawasaki et al., 1977; Dawis et al., 1985; Shirao et al., 1987). Though the pH of this injection is relatively low (2.5 to 4.5), it may be presumed that the pH in the blood would scarcely change after administration of this agent due to the small amount in the injection (2 mL) and buffer reaction in the blood, evoking no influences on the FO potential as well as in the SO potential (Maruiwa et al., 1992).

The agent's permeation into the intraocular portion is unclear, but MTCL passes through the blood-brain barrier (Schulze-Delrieu, 1979; Maruiwa et al., 1992). Thus it is thought that its permeation into the retinal side may be brought about through the blood-retinal barrier.

In the present study, the mean value of df_{FO} significantly increased between phase A (the initial 10 min before intravenous injection of 10 mg of MTCL) and phase B (the 10 min after injection) in the male and female groups ($P < 0.01$ and $P < 0.025$) and between phase A and phase C (the additional 10 min after injection) in both groups ($P < 0.01$ and $P < 0.05$) (Tables 1 and 2). This indicates that the effects of the dopamine receptor blocker on the FO potential were longer than expected.

It is widely accepted that the retinal neurotransmitter dopamine interacts with two major types of dopamine receptors: the D_1 and D_2 dopamine receptors (Kebabian and Calne, 1979). Each receptor has its own agonists and antagonists (Kebabian and Calne, 1979; Dubocovich and Weiner, 1985; Tran and Dickman, 1992).

In the mammalian retina, the D_1 dopamine receptors are mostly concentrated in the inner plexiform, the inner nuclear and ganglion cell layers; they are scarcely present in the outer nuclear layer or the photoreceptor inner and outer segments, while the D_2 dopamine receptors are present in the outer retinal layers—the rods, cones and the retinal pigment epithelium (Dearry and Brunside, 1988; Gallmore and Steinberg, 1990; Tran and Dickman, 1992).

The D_1 dopamine receptors are linked to the stimulation of adenylate cyclase and increase cAMP, whereas the D_2 dopamine receptors are coupled negatively to adenylate cyclase and decrease cAMP. That is, the D_1 and D_2 dopamine receptors are localized differentially in the retina to mediate different physiologic effects of dopamine (Tran and Dickman, 1992).

Thus it is supposed that a blockade of dopaminergic D_2 autoreceptor by MTCL may accelerate the release of endogenous dopamine from the inner retinal layers through negative feedback (Dubocovich and Weiner, 1985; Maruiwa et al., 1992; Tran and Dickman, 1992). Some endogenous dopamine would reach to the outer retinal layers by diffusion or through inter-plexiform cells in the retina (Nguyen-Legros et al., 1989; Tran and Dickman, 1992), and bring about a hyperpolarized change in the basal membrane of the retinal pigment epithelium associated with increased electric resistance of the basal membrane. At the same time, hyperpolaric response of visual cells to light stimuli suppressed by MTCL (Maruiwa et al., 1992) would bring about the decrease of sensitivity of visual cells to light stimulation, resulting in irregularly fluctuated FO patterns associated with increased FO potential and increase of the df_{FO} values in MTCL (10

mg)-administration in the present survey. However, it is thought that direct erethism by released endogeneous dopamine is a rare possibility in the retinal pigment epithelium.

Accordingly, it may be presumed that such a dopaminergic reaction in the outer retinal layers, especially in the retinal pigment epithelium which was observed in the present FO study, may be brought about by a direct effect of MTCL on the D_2 dopamine receptors in the retinal pigment epithelium even in man.

In the main examination, the mean level of df_{FO} of the female group was significantly higher than that of the male group in phase B ($P < 0.05$) (Table 3). As a control, the experimental procedure was performed with physiological saline administration, and no changes were observed. The data suggest that there exists some difference between young males and females concerning sensitivity to dopamine, as previously postulated by Nakao and others (1994) and that young females may show a higher-than-male sensitivity to dopamine in the occurrence of the FO potential, as partly demonstrated in the present study (Figs. 2 and 3).

The reason why a stronger reaction to dopamine is revealed in young females could be because: i) the physiologic effects of dopamine which are mediated by specific receptors on target neurons are stronger in females; ii) the sensitivity to dopamine itself is higher in females; and iii) specific dopamine receptors in the retina are more numerous in females than in males.

Further investigation on more test subjects is needed to clarify the exact reason and mechanisms causing this difference based on sex in the young generation concerning sensitivity to dopamine, with special emphasis on the difference in sex in much younger or older people, in addition to *in vivo* and *in vitro* animal experiments.

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