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Introduction

The ERP component N400 is known to be sensitive to semantic anomalies. In a word-matching task, N400 is elicited by a word that does not match the preceding context. The N400 effect is larger for semantic anomalies than for syntactic anomalies. The N400 effect is also larger for semantic anomalies than for syntactic anomalies. The N400 effect is also larger for semantic anomalies than for syntactic anomalies.

Running head: ERP and age

The present study examined the N400 effect in a word-matching task. The N400 effect was measured in a group of young adults and a group of older adults. The N400 effect was larger for semantic anomalies than for syntactic anomalies. The N400 effect was also larger for semantic anomalies than for syntactic anomalies. The N400 effect was also larger for semantic anomalies than for syntactic anomalies.

**Abstract**

ERPs (N400, LPC and CNV) were elicited in two sets of subjects grouped according to age (young vs. elderly) using a word-pair category matching paradigm. Each prime consisted of a Japanese noun (constructed from 2-4 characters of the *Hiragana*) followed by one Chinese character (*Kanji*) as the target, this latter representing one of five semantic categories. There were two equally probable target conditions: match or mismatch. Each target was preceded by a prime, either belonging to, or not belonging to, the same semantic category. The subjects were required to respond with a specified button press to the given target according to the condition. We found RTs to be longer in the elderly subjects and under the mismatch condition. N400 amplitude was reduced in the elderly subjects under the mismatch condition, and there was no difference between match and mismatch response, which were similar in amplitude to that under match condition for the young subjects. In addition, the CNV amplitudes were larger in the elderly subjects. These results suggested that functional changes in semantic processing through aging (larger semantic networks and diffuse semantic activation) were the

cause of this N400 reduction, attributing a subsidiary role to attentional disturbance. We also discuss the importance of taking age-related changes into consideration in clinical studies.

**Keywords:** ERP, N400, CNV, LPC, aging, semantic processing

## 1. Introduction

Over the last few decades, change in cognitive function brought about by aging has been widely researched. A large number of studies have been made on the effect of aging on several event-related brain potential (ERP) components (Harbin et al., 1984; Gunter et al., 1992; Polich et al., 1985; Marsh and Thompson, 1973).

The N400 was discovered in 1980 by Kutas and Hillyard (1980ab). They found this negative component to be evoked at around 400 ms after sentence endings featuring a semantically incongruent word (Kutas and Hillyard, 1980b); or a word that was semantically acceptable but unpredictable in the context of that sentence (Kutas and Hillyard, 1984). The results of these studies suggested that the N400 was related to semantic priming or activation (Kutas and Hillyard, 1984). The N400 can be elicited with a word-series paradigm (Harbin et al., 1984), paired-word paradigm (Bentin et al., 1985; Holcomb, 1988), pseudo-oddball word paradigm (Katayama et al., 1990) or categorization paradigm (Polich, 1985). Age related change in the

N400 has been investigated in several studies (Harbin et al., 1984). These suggested both an amplitude reduction and a latency prolongation of the N400 through aging (Gunter et al., 1992; Gunter et al., 1995; Gunter et al., 1996; Hamberger and Friedman, 1990).

Auditory P300 elicited by an "oddball" paradigm has also been studied to clarify change in cognitive function through aging. These studies found an increase in P300 latency with age, ranging from 1.1 to 1.8 ms/year (Goodin et al., 1978; Syndulko et al., 1982; Brown et al., 1983; Polich et al., 1985; Puce et al., 1989; Picton et al., 1984); and a decrease in P300 amplitude with age, ranging from 0.2 to 0.28  $\mu\text{V}/\text{year}$  (Goodin et al., 1978; Puce et al., 1989; Picton et al., 1984).

The CNV was first reported by Walter and his colleagues in 1964 (Walter et al., 1964), and several studies have shown this component to be sensitive to manipulation of expectancy (Walter, 1965), arousal (Hillyard and Galambos, 1967) and attention (Tecce and Scheff, 1969). The effect of age on the CNV has been an object of study for some time. There is, however, some discrepancy among the results of these studies: while several studies

showed change with age (Loveless and Sanford, 1974; Nakamura et al., 1979; Tecce et al., 1980), others did not (Marsh and Thompson, 1973). Michalewski et al (1980) suggests that "age effects on CNV are not ubiquitous and may vary with the experimental task (p.o)".

This paper is intended as an investigation into age-related changes in semantic processing using ERPs, especially the N400. We have already used the N400 in clinical examination (Miyamoto et al., 1995). Assessment of cognitive function in psychiatric and neurological diseases is important in determining treatment and psycho-social aid. Recently, the N400 has been used for the study of cognitive dysfunction in schizophrenia (Andrews et al., 1993; Koyama et al., 1994), epilepsy (Puce et al., 1991; Miyamoto et al., 1995), Alzheimer's disease (Hamberger et al., 1995; Ford et al., 1996) and aphasia (Ito et al., 1996; Hagoort et al., 1996). To establish a clinical application for the N400, it is necessary to know what effect age may have on it.

The paradigm used in this study was easy, therefore enabling the subjects to predict a target stimulus from a prime stimulus. This meant that even

subjects with cognitive disturbances could perform the required task easily. The ease of such a paradigm is important for its clinical application.

In this study, reaction time (RT), CNV and LPC (late positive component) were also investigated to obtain information on changes in semantic processing through aging.

## 2. Method

### 2.1. Subjects

The subjects consisted of twelve elderly males ranging in age from 62 to 68 years, with a mean age of 65.6 years. Their length of education was more than 11 years and their Mini-Mental State (MMS) (Folstein et al., 1975) scores ranged from 25 to 30, with a mean score of 28, indicating that all the subjects were within the normal range. (Galasko et al., 1990). In addition, twelve male students ranging in age from 21 to 26 years (mean = 24.0 years) were recruited from Hokkaido University. All the subjects, in both groups, had normal, or corrected to normal, vision and were right-handed, except for one elderly subject who was possibly ambidextrous. None of them had any history of

neurological or psychiatric disorder. All the subjects were remunerated.

## 2.2. Design and Procedure

A category matching paradigm was used to elicit ERPs, in which each trial consisted of a warning sign, a prime and a target stimulus. The warning sign was a double-circle; the prime consisted of 2 to 4 characters taken from the *Hiragana* (one of the Japanese syllabaries) making a word selected from a list of 35 nouns (7 nouns per semantic category); the target consisted of a Chinese character-or "Kanji" in Japanese-indicating one of five semantic categories-color, tree, fish, bird or insect<sup>1</sup>. The following two stimulus conditions were presented according to the semantic relationship between a prime and its following target: (1) a match condition-in which the target was preceded by a prime belonging to the same semantic category, or (2) a mismatch condition-in which the target was preceded by a prime belonging to a different semantic category (Figure 1). Each condition was presented in random order with a probability of 50%. Each subject participated in five blocks of 20

trials. There were 20 - 40 practice trials prior to the first experimental block.

The start of each trial was signaled by a warning stimulus with a duration of 1000 ms. This was followed 1040 ms later by the prime and target stimuli in succession, both of which lasted 400 ms with an onset-to-onset interval of 1040 ms. Each target stimulus was followed by a 1040 ms delay before the onset of the warning stimulus for the next trial. The stimuli subtended a vertical visual length of 5 mm, and a horizontal length ranging from 5 to 20 mm. Stimulus presentation was controlled using a personal computer (NEC PC-9801 Vm).

Subjects were seated approximately 80 cm away from the CRT display (NEC PC-KD852). They were instructed to press a key switch to match-condition targets with one thumb and to mismatch-condition targets with the other thumb, as quickly as possible. The assignment of response hands was counterbalanced across the subjects. They were also requested to refrain from blinking, except during the presentation of the warning sign.

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Insert Figure 1 around here  
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### 2.3. Recording and analysis

We analyzed EEGs recorded from Fz, Cz, and Pz electrodes, all of which were referred to linked ear lobes. Impedances were kept below 5 k $\Omega$ . The bandpass was set at 0.04-30 Hz (NEC San-ei 1A98), and the EOG was monitored to exclude epochs contaminated with blinks or eye movements from the analysis. EEGs were digitized off-line with a personal computer (NEC PC-H98). ERPs for the prime and target stimuli were averaged off-line for 2400 ms with a 200 ms baseline before the prime stimulus onset (sampling rate = 250 Hz). Those for the target stimuli were also averaged off-line for 1000 ms with a 200 ms baseline before the target stimulus onset (sampling rate = 500 Hz). Trials with artifacts, and those with response errors or omissions, were excluded from the ERP averaging. All subjects made at least 25 good trials under each condition.

The N400 mean amplitudes were measured as the mean voltage between 226 and 276 ms under the match condition, and between 276 and 326 ms under the mismatch condition in the young subjects; and between 276 and 326 ms under both conditions in the elderly subjects, relative to a 200 ms baseline before the target stimulus onset. The LPC mean

amplitudes were measured as the mean voltage between 326 and 376 ms under the match condition, and between 476 and 526 ms under the mismatch condition in the young subjects; and between 376 and 426 ms under the match condition and between 576 and 626 ms under the mismatch condition in the elderly subjects, relative to a 200 ms baseline before the target stimulus onset. Finally, the CNV mean amplitude was measured as the mean voltage between 1200 and 1400 ms after the prime stimulus onset, relative to a 200 ms baseline before the prime stimulus onset.

We used analysis of variance (ANOVA) for statistical analysis, and vector analysis to assess scalp distribution differences between the two groups and between conditions (McCarthy and Wood, 1985). Greenhouse and Geisser correction was employed where appropriate. We employed the Tukey method for post-hoc comparison, with a significance level of  $p < 0.05$ .

### 3. Results

#### 3.1. Behavioral data

Table 1 shows the mean RTs and error rates for each condition in both age groups. These were analyzed with a 2-factor (2 ages [young vs. elderly] X 2 conditions [match vs. mismatch]) ANOVA. RTs were longer for the elderly subjects ( $F(1,22)=14.85$ ,  $p<0.001$ ), and under the mismatch condition ( $F(1,22)=27.40$ ,  $p<0.001$ ). The interaction was not significant. The error rates showed only the effect of age: being larger in the elderly subjects ( $F(1,22)=6.64$ ,  $p<0.02$ ).

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Insert Table 1 around here  
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#### 3.2. ERP data

Figure 2 shows the grand average ERPs for the primes and targets; and Figure 3 shows the grand average ERPs for the targets. In those for the primes and targets, the CNVs were larger in the elderly subjects and no difference was found between stimulus conditions in either age group. In the young subjects' grand average ERPs for the targets,

the prominent negative-going component peaked at around 250 ms under the match condition and around at 350 ms under the mismatch condition, corresponding to that for the N400. The N400 had a larger amplitude and a longer duration under the mismatch condition. The LPC followed the N400 under both conditions.

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Insert Figure 2 and 3 around here  
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### 3.2.1. N400 Amplitude

Figure 4 shows the mean amplitude of N400 for each condition in both age groups. The N400 data were analyzed with a 3-factor (2 ages X 2 conditions X 3 electrode site [Fz, Cz, and Pz]) ANOVA. The effect of site was significant ( $F(2,22)=4.08$ ,  $p<0.05$ ,  $e=0.743$ ). Interaction between condition X site ( $F(2,44)=31.04$ ,  $p<0.001$ ,  $e=0.652$ ) and among age X condition X sites ( $F(2,44)=15.02$ ,  $p<0.001$ ,  $e=0.652$ ) was also significant. The effect of age, however, was not significant ( $F<1.0$ ). Subsequent tests indicated that this significant interaction among age X condition X site arose from the fact that

differences between the conditions were significant only in the young group; N400 amplitude was larger at Fz and Cz under the mismatch, and the difference between age groups was significant only under the mismatch condition; N400 amplitude was larger at Fz in the young subjects. N400 amplitudes under both conditions in the elderly subjects were almost same, and were almost identical to that under match condition in the young subjects.

In order to assess scalp distribution difference between the two age groups, and between conditions, the N400 amplitude was re-analyzed after the data had been normalized by vector length. By so doing, both group and condition effects were normalized and scalp topography information alone could be compared across experimental conditions. Analysis of these N400 amplitude vectors confirmed two of the interactions stated above: condition X site ( $F(2,44)=31.7, p<0.001, e=0.693$ ) and age X condition X site ( $F(2,44)=22.64, p<0.001, e=0.693$ ) were significant.

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Insert Figure 4 around here  
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### 3.2.2.LPC amplitude

Figure 5 shows the mean amplitude of LPC for each condition in both age groups. The LPC data were analyzed with a 3-factor (2 ages X 2 conditions X 3 electrode sites [Fz, Cz, and Pz]) ANOVA. Analysis of the LPC amplitudes indicated that they were larger at Pz than at Fz ( $F(2,44)=18.81, p<0.001, e=0.677$ ), and an interaction between age X site was significant ( $F(2,44)=5.59, p<0.02, e=0.677$ ). This was due to the fact that the effect for site was significant only in the young subjects in subsequent tests.

Analysis of the LPC amplitude vectors confirmed an interaction between age X site ( $F(2,44)=5.59, p<0.01, e=0.677$ ).

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Insert Figure 5 around here  
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### 3.2.3.CNV amplitude

Figure 6 shows the mean amplitudes of CNV in both age groups. The CNV data were analyzed with a 2 ages X 3 electrode sites ANOVA. The CNV amplitudes in the

elderly subjects were larger ( $F(1,22)=4.71, p<0.05$ ), and the amplitude at Cz and Pz was larger than at Fz ( $F(2,44)=33.10, p<0.001, e=0.55$ ).

Analysis of the CNV amplitude vectors indicated an interaction between age X site ( $F(2,22)=1.53, p<0.05, e=0.54$ ).

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Insert Figure 6 around here  
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#### 4. Discussion

In this study, RTs were found to be longer in elderly subjects. Wilkinson and Allison (1989) have reported an age effect for simple RTs in 5,325 subjects. Age differences in RTs in the present study (232.6 ms) were larger than in their study (36.2 ms). This can be explained in terms of differences in semantic processing according to age. That is to say, elderly subjects require more time for semantic processing under either stimulus condition and accuracy is poorer. What these behavioral data make clear is that elderly subjects exhibit age-related changes in semantic processing.

In the present study, the N400 was observed as a negative-going waveform that occurred with a latency of around 300-350 ms, showing a rather earlier latency than the original N400 of Kutas and Hillyard (1980b). The reason for this may be that a paired-word paradigm was used in this study, instead of a sentence paradigm (Holcomb, 1988; Kuperman et al., 1995). In the present study, the N400 amplitude was only larger in the young subjects under the mismatch condition, and was almost identical under the match condition. This means that there was no significant difference in N400 amplitude between either stimulus condition in the elderly subjects.

The LPC is a positive-going component following the N400. This component is elicited large by paradigms utilizing button-press tasks (Polich, 1985). Several researchers have described the LPC as the P300 (Polich, 1985). However, although there is a close relationship between the LPC and the P300, it is rather debatable as to whether the nature of both components is identical (Puce et al., 1991). The LPC was most prominent under the match condition in the young subjects, but no significant difference in LPC amplitude between age groups was observed.

Although several studies have found a reduction in CNV amplitude through aging (Loveless and Sanford, 1974), it was larger in the elderly subjects in this study. One possible explanation for this may lie in the particular strategy taken by each group for the paradigm. It is possible that the young subjects had memorized all of the five target words during the early part of the experiment and were thus easily able to predict the words for the targets in each trial; the elderly subjects, however, not having memorized the target words, would have been unable to do so. The young subjects would, therefore, have been freer to pay less attention to the targets themselves; while the elderly subjects probably had to pay more attention to the targets, thus eliciting larger CNVs. However, the elderly subjects elicited smaller N400s under the mismatch condition. This finding suggests that this reduction in N400 amplitudes under the mismatch condition in the elderly subjects was not due to attention disturbances in the present study; although the N400 has exhibited such a relationship to attention in previous research (McCarthy and Nobre, 1993, Koyama and Kakigi, 1996).

This leads us to further consider the reasons for this N400 reduction in elderly subjects. There are several possible reasons for this difference in semantic priming effect between the two groups: first, this reduction in N400 may be explained by a difference in semantic network between each age group (Gunter et al., 1992): these researchers suggested that larger semantic networks, in which language stimuli take at least twice as long to be processed by elderly people, cause a diffuse semantic activation in that age group, thus reducing N400 amplitudes for unexpected words. Another possible explanation for N400 reduction in the elderly subjects may lie in structural changes in the brain through aging. Research has revealed atrophy (Sullivan et al., 1995) and a reduction of glucose metabolism (Eberling et al., 1995) in the temporal lobes through aging. Several studies have reported that anterior medial temporal regions were generators of N400 (Puce et al., 1991; McCarthy et al., 1995; Nobre and McCarthy, 1995). Therefore, it is possible that the N400 generators had changed through aging.

In this study, N400 amplitudes were only reduced in the elderly subjects under the mismatch

condition, and were almost identical with those for the young subjects under the match condition. This result suggests that the functional changes given in the first reason stated above may, therefore, have been the cause of this N400 reduction in the elderly subjects under the mismatch condition. Although there is possibly some change in N400 generator, we have no definite information on any structural change.

The easy paradigm used in this study was enabled the subjects to predict a target stimulus from a prime stimulus. we have already used the N400 for clinical examination where ease of paradigm is important, so that even subjects with cognitive disturbances may perform it.

To summarize, this study aimed at clarifying age-related changes in semantic processing with ERPs. N400 amplitudes were found to be reduced under the mismatch condition in the elderly subjects. This means that semantic activation was diffuse in this group, possibly because of larger semantic networks than that of young subjects. It was also found that attentional disturbance was not the main factor in this N400 reduction. From these results, it is clear that age-related changes should be taken into

consideration when the N400 is to be used in  
clinical studies.

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**Footnote**

The Japanese writing system consists of three sets of symbols: the *Kanji* and two types of syllabary—the *Hiragana* and the *Katakana*. In general, the *Kanji* are used to represent words or their semantic components, while syllabaries are used to represent the sounds of the language.

Table 1: Reaction times and Error rates

Stimulus condition	Young	Elderly
	Reaction times (ms)	
Match	470.3 (87.53)	675.2 (184.4)
Mismatch	521.4 (92.32)	781.6 (206.7)
	Error rates (%)	
Match	0.54 (0.54)	1.46 (1.16)
Mismatch	0.50 (0.77)	1.29 (1.12)

Note: Standard deviations are given in parentheses.

### Figure Legends

**Fig. 1.** Exemplar of prime and target stimulus under each condition. Prime stimuli were written in the Japanese syllabary, *Hiragana*, and target stimuli in Chinese characters, or *Kanji*. An English translation of the stimuli is given in parentheses.

**Fig. 2.** Grand averaged ERPs for the prime and target stimulus. Solid lines show ERPs in the young subjects, and broken lines show those in the elderly subjects. On the scale, the left arrow indicates time of prime stimulus presentation, and the right arrow indicates time of target stimulus presentation.

**Fig. 3.** Grand averaged ERPs for the target stimulus. Solid lines show ERPs under the mismatch condition, and broken lines show those under the match condition. On the scale, the arrow indicates time of target stimulus presentation.

**Fig. 4.** Mean N400 amplitudes. Solid lines show the mean N400 amplitudes under the mismatch condition, and broken lines show those under the match condition. Error bars show S.D.. The N400 mean amplitudes were measured as the mean voltage between 226 and 276 ms under match condition, and between

276 and 326 ms under mismatch condition in the young subjects; and between 276 and 326 ms under both conditions in the elderly subjects, relative to a 200 ms baseline before the target stimulus onset.

**Fig. 5.** Mean LPC amplitudes. Solid lines show the mean LPC amplitudes under the mismatch condition, and broken lines show those under the match condition. Error bars show S.D.. The late positive component (LPC) mean amplitudes were measured as the mean voltage between 326 and 376 ms under match condition, and between 476 and 526 ms under mismatch condition in the young subjects; and between 376 and 426 ms under match condition, and between 576 and 626 ms under mismatch condition in the elderly subjects, relative to a 200 ms baseline before the target stimulus onset.

**Fig. 6.** Mean CNV amplitudes. Error bars show S.D.. The CNV mean amplitude was measured as the mean voltage between 1200 and 1400 ms after the prime stimulus onset, relative to a 200 ms baseline before the prime stimulus onset.

Exemplar of stimulus

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Stimulus	Exemplar
Condition	prime - target

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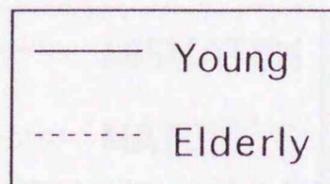
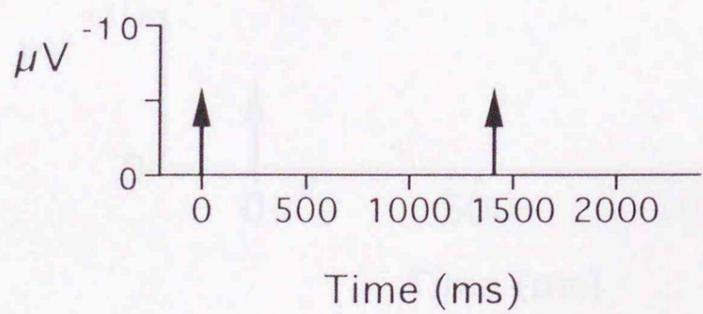
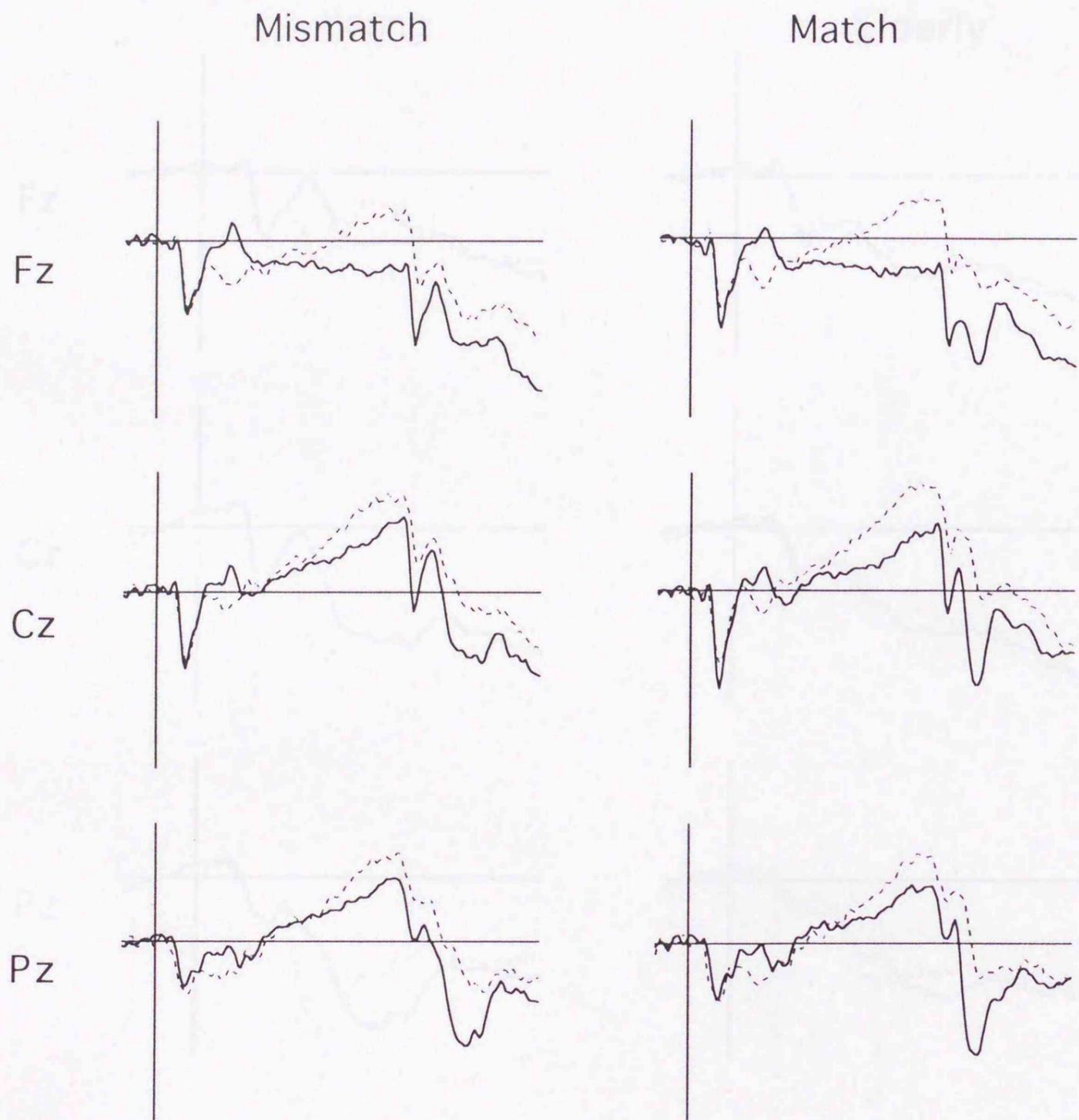
Match      からす - 鳥  
              ( crow - bird )

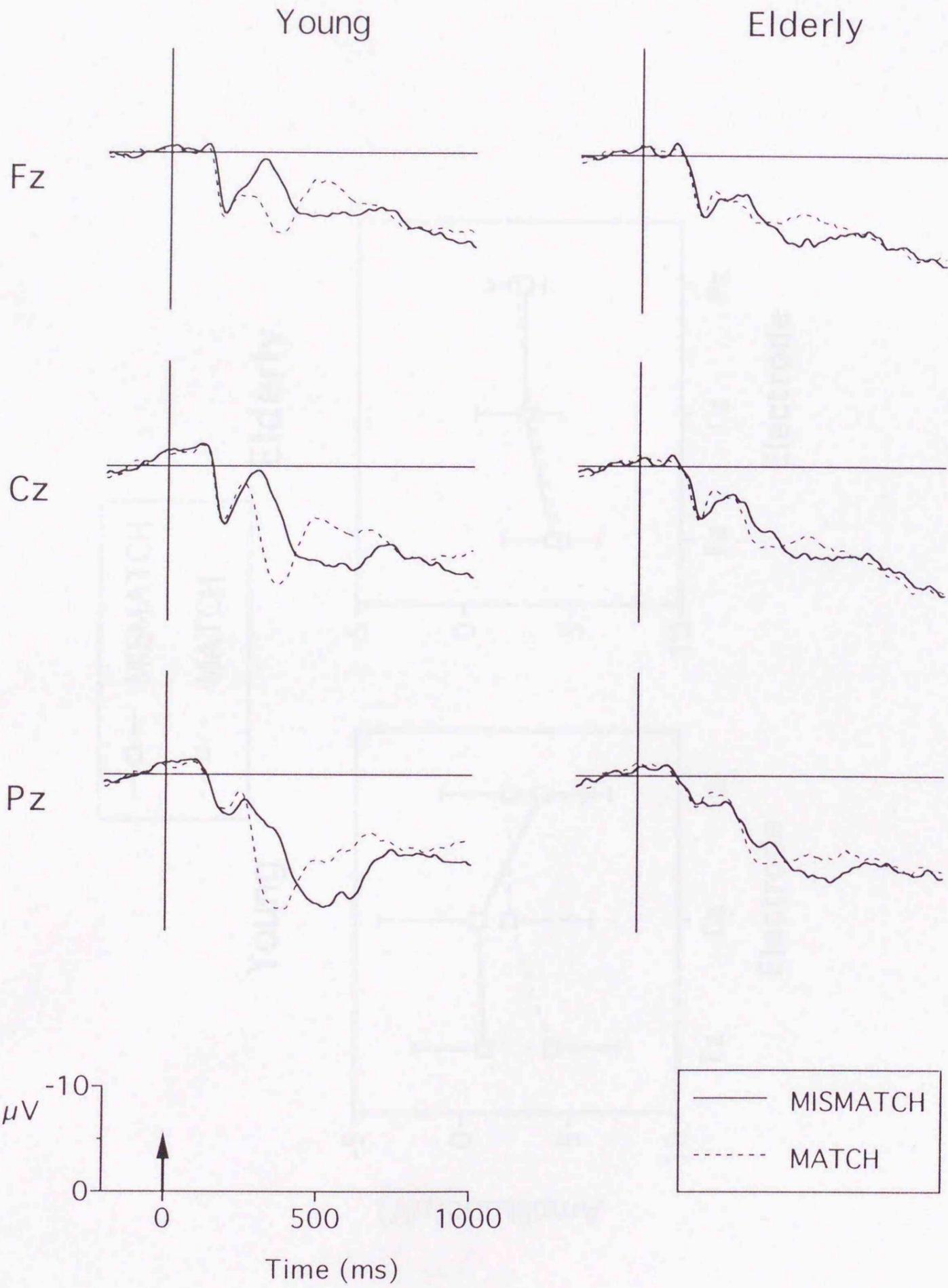
Mismatch      とんぼ - 木  
                  ( dragonfly - tree )

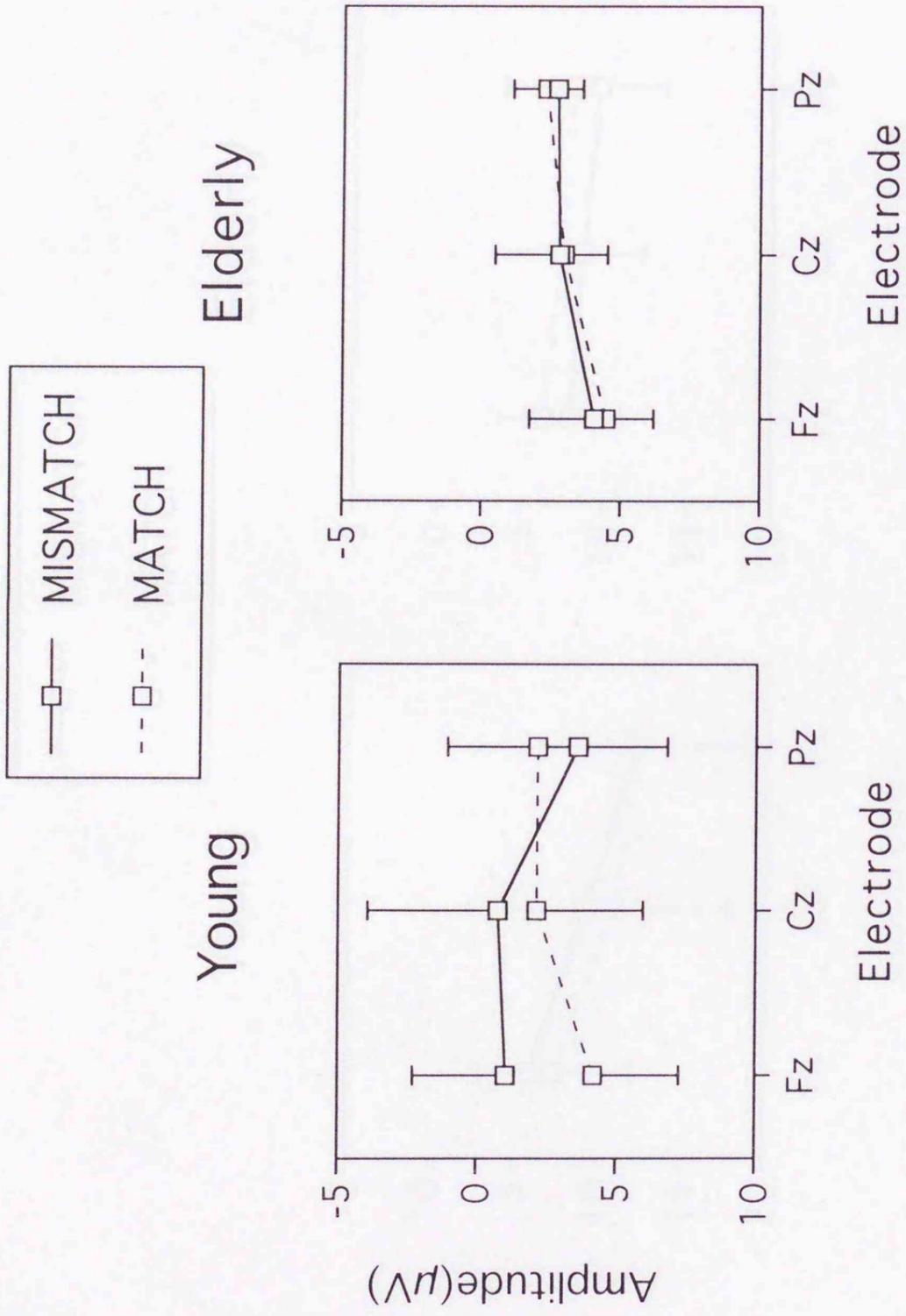
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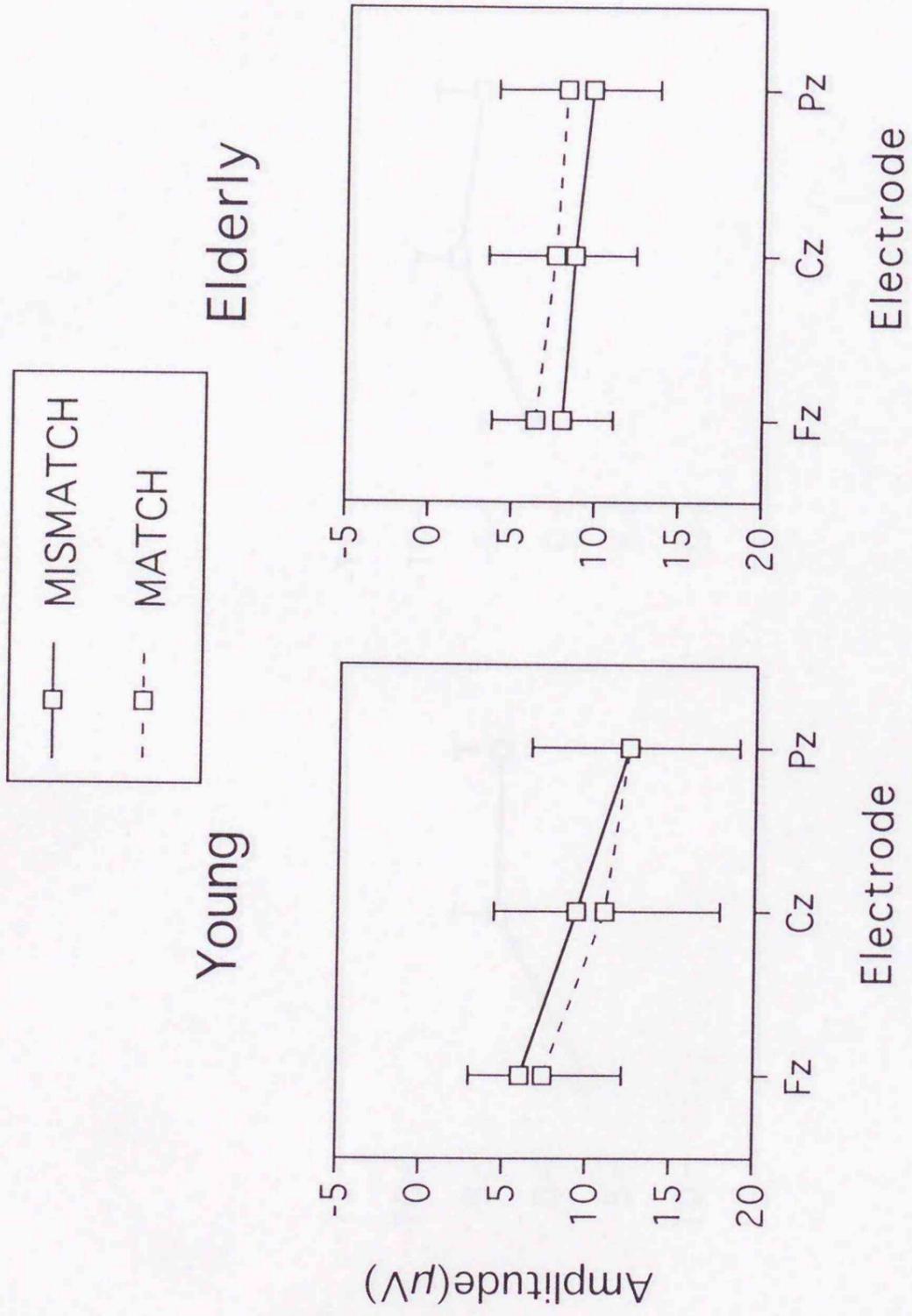
Mismatch

Match

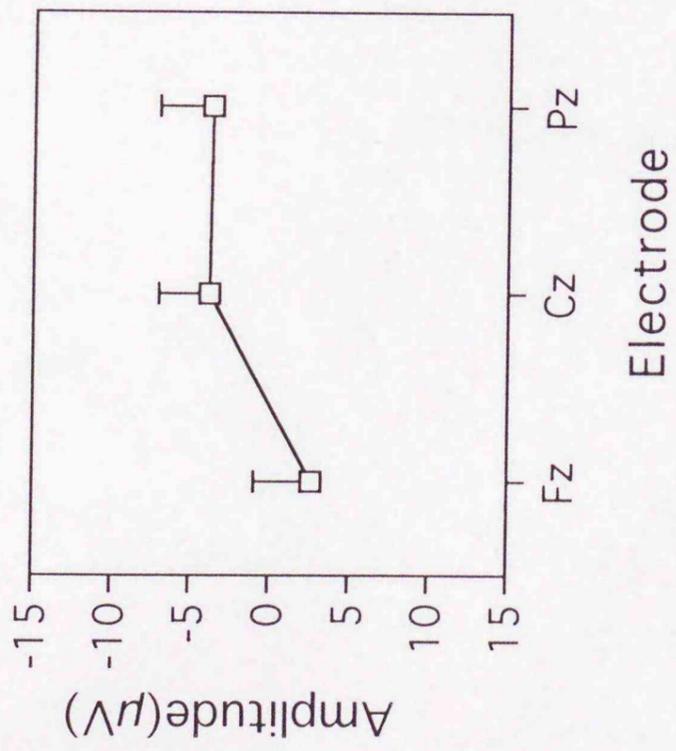




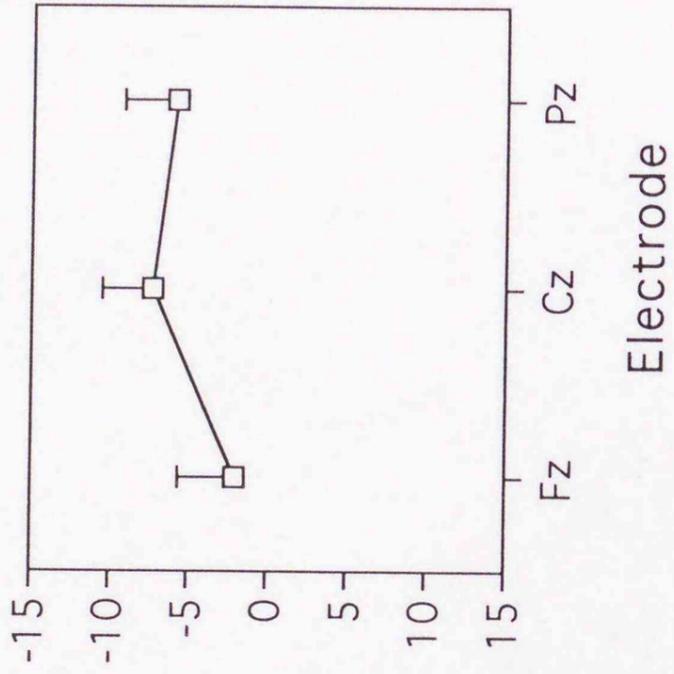


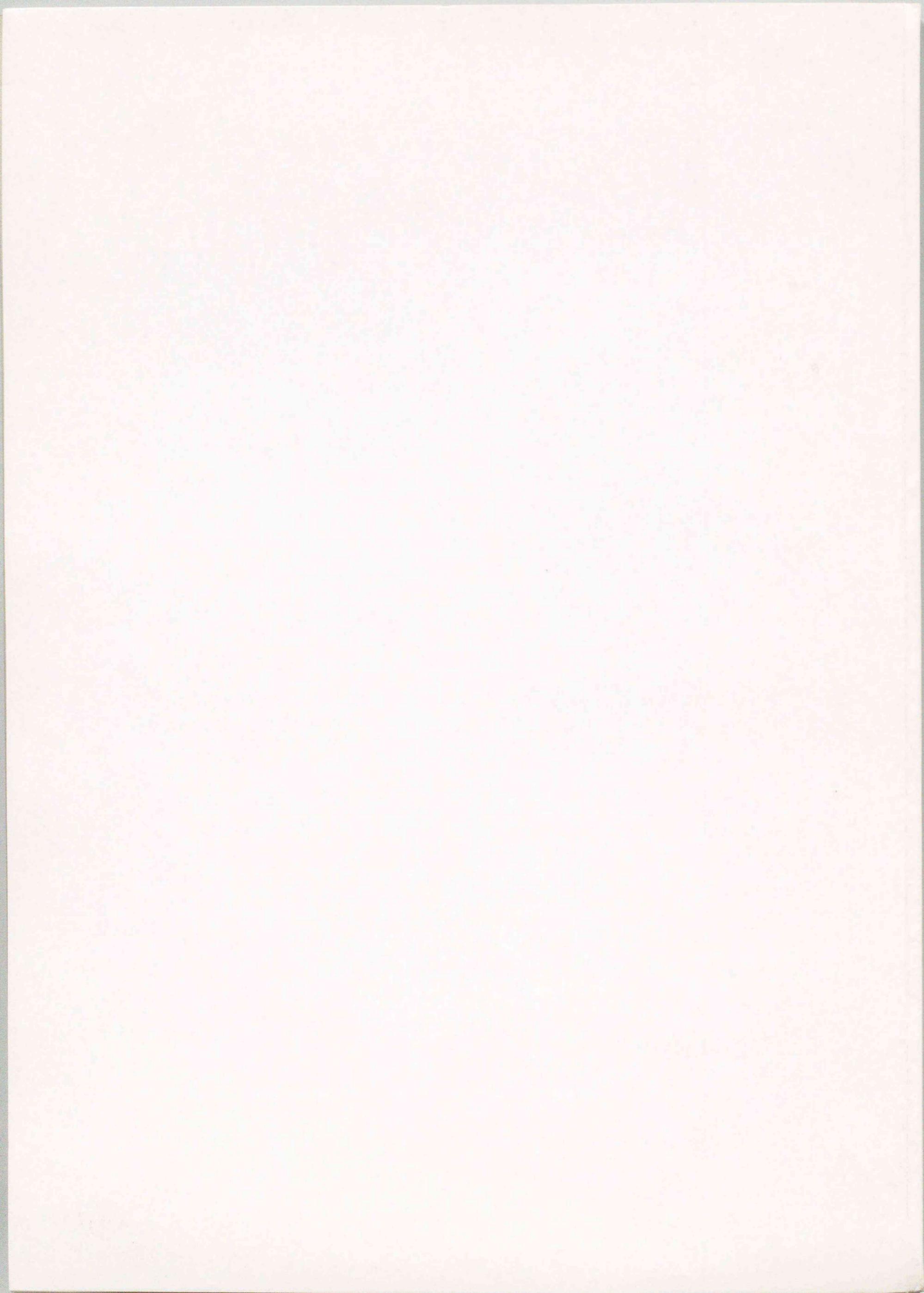


Young



Elderly



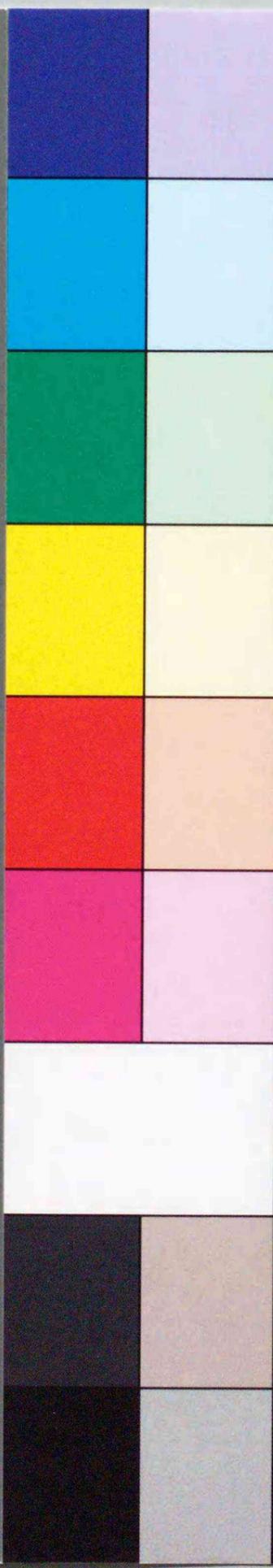


Inches 1 2 3 4 5 6 7 8  
cm 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

# Kodak Color Control Patches

© Kodak, 2007 TM: Kodak

Blue Cyan Green Yellow Red Magenta White 3/Color Black



# Kodak Gray Scale



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A 1 2 3 4 5 6 M 8 9 10 11 12 13 14 15 B 17 18 19

