

Age related sex difference in higher cognitive abilities of healthy middle and old age people

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中高年者の高次認知機能の性差について

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要約

日本人中高年者の知覚情報処理、言語記憶、言語流暢性の性差について発達心理学的な検討を加えた。住民検診に参加した40歳から89歳までの男女512名が対象者であった。知覚情報処理、言語記憶、言語流暢性のすべての指標において年齢と性との間の交互作用は有意であった。数字末梢検査における知覚情報処理、言語記憶、言語流暢性では40歳代では性差が認められたが50歳代以降では性差は見られなかった。記憶検査では同様に40歳代での性差は50歳代以降では消失した。言語流暢性検査では60歳代でのみ性差が見られた。若年者では高次認知機能に性差の存在が指摘されてきたが、本研究の結果からはそれらの性差は発達の定常ではないことを示している。これらの結果は性ホルモンが前頭葉機能を主とする認知機能に寄与していることを示唆する。

Key words

sex difference, higher cognitive function, aging, frontal cortex, sex-related hormone

1. Introduction

It is commonly accepted that a difference exists between male and female in cognitive abilities. The difference in the academic achievement of boys' and girls' SAT scores (Scholastic Achievement Test) showed that mean grades of the girls in English and foreign languages are considerable higher than those of boys, whereas the grades of the boys are barely higher than those of girls in mathematics and physical science (Krausmeier, 1985). Maccoby (1966) reviewed approximately 1600 articles that provided information about psychological sex difference and arrived at conclusions regarding sex differences: girls are higher than boys in verbal abilities, such as reading, vocabulary comprehension, and spelling. He also found that boys are higher than girls in spatial abilities, quantitative abilities, and aggressiveness (Maccoby and Jacklin, 1974). The female advantage of verbal abilities has been reported in various facets such as in spelling (Feingold, 1988), verbal fluency (Kimura, 1994), reading (Kimura, Saucier, & Matuk, 1996), verbal memory (Stumpf & Jackson, 1994), and visual memory (Harshman, Hampton, & Berenbaum, 1983). Krausmeier (1985) reported a sex difference in verbal ability in 40 boys and 40 girls of 10-year old children. The results showed a superiority of girls over boys. The mean verbal ability of boys was 122.2 (range from 72 to 149) whereas that of the girls was 132.6 (range from 82 to 157).

Long debates of nature and nurture problem clearly point

out that biological factors seem more strongly related to cognitive abilities than environmental factors (see Caplan, Crawford, Hyde, & Richardson, 1997 for the nurture view). For example, Kimura (1999) reviewed studies and concluded that the most sexually differentiated functions are strongly influenced by early and/or concurrent hormonal environments.

Almost all evidence that contributed to the debates was from the behavioral data of children and young adults, that is, they are all from the examination of early stage human development. It is not clear, however, whether a sex difference in cognitive abilities remains stable throughout human life or if it changes in the middle or at a later stage of human development due to the influences of various environmental factors, such as education in school, working experiences, encountered events in daily life and biological factors such as hormonal environments.

The background of this inquiry comes from several recent findings in brain science that learning experiences or environmental factors affect the brain function, especially the prefrontal cortex related function such as attention, memory and verbal ability.

First, neuropsychological findings by brain damaged case studies, behavioral studies, and brain-imaging methods showed that cognitive abilities such as attention, memory, and verbal function in humans strongly related to the systematic function of prefrontal cortex, sub-cortex and cerebellum (Gazzaniga, 2005; Hatta, 2003; Hatta, Hasegawa, & Wanner, 2004; Hatta, Ito & Yoshizaki, 2001; Hatta, Masui, Ito, Ito, Hasegawa, & Matsuyama, 2004; Ito, 1998).

Second, recent brain-imaging studies also revealed a system-

atic relationship between the prefrontal cortex and sub-cortex. This indicates that an emotional experience evoked by environmental factors may affect the process of cognitive abilities. It is also hypothesized that since emotional experiences brought on by environmental factors are different between both sexes, cognitive abilities in male and female are differentially affected by these environmental factors. For example, it became clear that learning experiences of strong fear (or environmental factors that are causes of mental trauma) could modify the way the prefrontal cortex functions. Some robust evidence exists indicating a relationship between the subcortex (e.g., amygdala and hypothalamus) and cognition. Recent studies on amygdala by the introduction of brain imaging techniques suggest that there are complex interactions between neural systems. For example, a recent review of the role of subcortex by Pherips (2004) showed that cognition and awareness (attention) influenced amygdala in many ways. That is, verbal communication of thought processes associated with fear can alter the amygdala function and the expression of this learning depends on amygdala.

This means that the subcortex plays a role in the expression of fears or hormonal secretion and that these expressions are generated through imagination (that is, cognition). Therefore, it is possible to postulate that emotional reactions (or hormonal secretion) by learning experiences (or life events in a later human developmental stage such as environmental factors) can differentially modulate prefrontal cortex function such as attention, memory and verbal function between males and females. A very recent review by Steinberg (2005) claimed similar issue and suggested convenient references.

The first purpose of this study was to examine the relationship of sex difference with perceptual speed, verbal fluency and memory function in normal middle and old age people. More concretely, this study aimed to examine if there is a sex difference even in late stage of human development as well as documented at the early stage of human development.

The second purpose of this study was to examine the validity of Kimura's model for sex and cognition. As described earlier, Kimura (1999) proposed that most of the sexual evident differentiated functions are strongly influenced by the amount of hormonal secretion (or subcortex function). She strongly stressed a critical role of estrogen in the verbal ability and perceptual speed. If her model is valid, a sex difference such as female superiority in verbal ability must not remain stable after menopause. We may be able to expect no sex difference after the age of around 50 years old.

2. Method

2.1 Participants

Five hundred and twelve (315 females and 197 males) community dwellers participated in this study. The cognitive tests such as the D-CAT (Digit Cancellation Test, Hatta, Ito, & Yoshizaki, 2001) for attention and logical delayed memory

were administered as a part of an ongoing cohort study (Nagoya University Yakumo Project which started from 1982) set in the Yakumo Town, a rural farming community, of Hokkaido district. Samples from Iwakura City, a satellite city of Nagoya, were also included to control the sampling bias. The background and methods of the cohort study are reported in greater detail elsewhere (Aoki, & Ito, 1999). This study analyzed only the D-CAT data given in August 2003. All the data in this analysis was obtained from volunteers who had no neurological or psychological anamneses. Table 1 shows the participants' demographic data. Participants were classified into 4 age groups, 40's, 50's, 60's, and over 70's age groups. Official statistics as for the discrete mean climacteric age in Japanese women does not exist; however, it has been reported that it must be around 50 years old (Taketani & Maehara, 2001). In females, the 40's age group is regarded as pre-climacteric and all groups after 50 years old are regarded as the post-climacteric group. All of the participants were ordinary healthy citizens. The participants showed no signs of physical disorders, internal disease, or of dementia at the time of examination in August 2003. For signs of internal diseases, the participants were examined by physicians in accordance with the health examination program, and they were tested for signs of mild dementia or other neurological defects by the neuropsychologists using tests such as the Clock Drawing, D-CAT, memory, Stroop, Money road, and the QOL (quality of life) tests. The selection criteria for including data analysis were as follows: in the Clock Drawing Test (Rouleau, Salmon, & Butters, 1992), any respondents with mild dementia or dementia (more than 4 points according to the Japanese criteria by Nagahama, et al., 2001) were excluded. Since the Clock drawing test is not regarded as a sensitive measure of mild dementia, participants whose performance was less than 2 SD from the mean in the memory, Stroop, and Money road tests were also excluded because they were given the suggestion by the Yakumo Town cohort project administration office to visit hospital for precise examination. Thus, 20 participants were deleted from the data analysis.

All participants were given an informed consent sheet and only those who agreed with participation were included. Well-trained examiners administered the D-CAT, verbal fluency test and memory test.

Table 1: Demographic data of participants. Number of participants and mean years of education

Age	40's	50's	60's	70's+	Total
Male	27	46	72	52	197
Years of Educ.	11.81	11.33	9.86	8.88	
Female	55	105	104	51	315
Years of Educ.	12.00	11.03	9.70	8.35	
Total	82	151	176	103	512

2.2 Materials and procedure

2.2.1 Perceptual speed

To examine perceptual speed, this study employed the D-CAT test (Hatta, Ito & Yoshizaki, 2000). The test sheet consisted of 12 rows of 50 digits. Each row contained 5 sets of the numbers 0 to 9 arranged in random order. Thus any one digit would appear 5 times in each row with randomly determined neighbors. The D-CAT as a whole consisted of three such sheets. Participants were instructed to search for the target number(s) that had been specified to them and to delete each one with a slash mark as fast and as accurately as possible until the experimenter sent a stop signal. There were 3 trials, first with a single target number (6), second with two target numbers (9 and 4), and third with three (8, 3, and 7). Each trial was allowed 1 minute; hence the total time required for D-CAT was 3 minutes. In the second and third trials, it stressed that all of the target numbers instructed should be cancelled without omission. The D-CAT basically follows the attention model proposed by Sohlberg and Mateer (1989), where they proposed hierarchical classifications; each component of the hierarchy requires the effective functioning of the one below it. The D-CAT aimed to evaluate three levels of attention, *focused attention*, *sustained attention concentration* and *selective attention*. Several measures of D-CAT, *Hit 1*, *Hit 2* and *Hit 3*, and the *Omission* ratio were calculated in accordance with the test manual.

In this study, two measures of D-CAT, *Hit 1* and *Hit 3* were used to examine perceptual speed. *Hit* is one of the indices of the D-CAT and it refers to the total number of digits the participant inspected and deleted. This relates mainly to the components such as the information processing speed, focused attention, and sustained attention. *Hit 1* refers to the total number of digits the participant slashed in one target digit condition. *Hit 3* refers to the total number of digits the participants cancelled in three digits target condition. This also relates to the components such as the information processing speed and focused attention and this study maintains that there was more engagement of sustained attention or working memory in the three digits condition, *Hit 3*, than one digit target condition, *Hit 1*. *Omission* ratio is also one of the indices of D-CAT and it reflects components mainly such as sustained attention and selective attention. *Omission* ratio was too small one (less than 0.01 %), hence we do not refer to it in this study. The rationale, validity and reliability of D-CAT as an attention test are evident elsewhere (Hatta, Ito, & Yoshizaki, 2005).

2.2.2 Verbal memory

The delayed logical memory test Japanese version (Wechsler's Memory Scale-R: Japanese version, Sugishita, 2002), which consisted of 25 segments, was given as *logical memory*. The participants were asked to recall the short story. They received no prompting. After several cognitive test items including the D-CAT were compiled, participants were asked to remember the

given story as correctly as possible. The mean memory interval in logical memory recall was 15-17 minutes. The interval was not necessarily identical among the participants; however, all cases involve some long-term memory stage.

2.2.3 Verbal fluency

The examiner administered Japanese letter fluency test (Japanese version by Ito & Hatta, 2001). The participants were asked to generate Japanese nouns that begin with each letter, /a/, /ka/, and /shi/, as many as possible for 60 seconds for each letter. The examiners noted inhibition when subjects reported proper nouns. The examiners instructed the participants to not repeat the same words they reported earlier. The examiners measured the total number of generated nouns for the letters.

The same examiner administered the D-CAT, logical memory and letter fluency tests for each participant as a part of the neuropsychological examination of the Yakumo project.

3. Results

Table 2 and Figure 1 show *Hit 1* performance rates of male and female participants for the D-CAT as a function of their age group. This paper conducted MANCOVA (covariate variable was years of education, dependent variables were *Hit 1*, *Hit 3*, *logical memory* and *letter fluency*). Since there was a relatively high correlation between the years of education and the employed measures, a variable for the total years of education was treated as a covariate variable ($r = 0.35, 0.30, 0.29, \text{ and } 0.32$; *Hit*

Table 2: Mean score and SD of the *Hit 1* scores as a function of age group

Age	40's	50's	60's	70's+
Male Mean	28.93	27.52	22.92	20.48
SD	5.54	5.38	6.43	4.07
Female Mean	32.15	29.06	23.02	23.02
SD	7.04	6.58	4.50	5.30

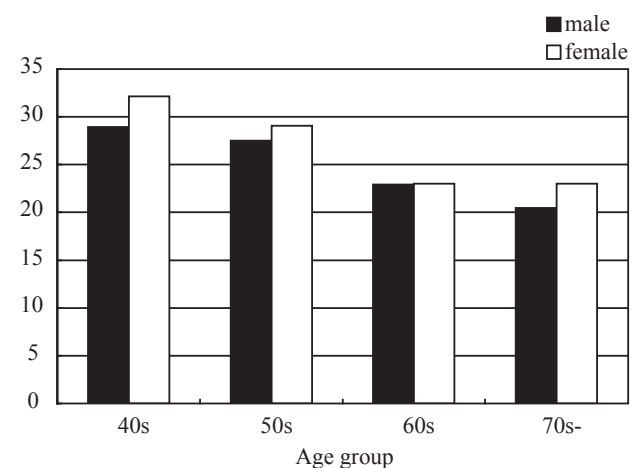


Figure 1: Sex difference in perceptual speed by *Hit 1*

1, *Hit 3*, *logical memory* and *letter fluency*, respectively). This paper shows significant results for the results of MANCOVA test indicating strong factors in sex and age groups (Wilks $\lambda = 0.77$, Rao 'R = 11.62, df = 12, 1323, $p < 0.001$: age group, Wilks $\lambda = 0.97$, Rao 'R = 3.62, df = 4, 500, $p < 0.001$: sex). The interaction between sex and age groups was also significant (Wilks $\lambda = 0.95$, Rao 'R = 2.36, df = 12, 1323, $p < 0.005$). This means that the performances of males and females were not parallel from middle to old age people. Since the interaction was significant, we conducted post hoc analyses (by Neuman-Keuls test) for each measure. The results are as follows.

3.1 Hit 1

The performance of the 40's age group was better than that of 50's ($p < 0.001$), performance of 50's age group was better than that of 60's ($p < 0.001$), and performance of 60's age group was better than that of 70's+ ($p < 0.001$). In other words, the perceptual speed in single target inspection decreased gradually from the 40's. The sex difference in *Hit 1* performance showed up only in 40's age group ($p < 0.001$), whereas there was no significant sex difference in the other age groups (50's, $p < 0.30$; 60's, $p < 0.92$); and 70's+, $p < 0.29$, respectively).

3.2 Hit 3

Table 3 and Figure 2 show *Hit 3* performance of male and female participants in D-CAT as a function of age group. The performance of the 40's age group was better than that of the 50's age group ($p < 0.001$), performance of the 50's age group was better than that of the 60's age group ($p < 0.001$), the 60's age

Table 3: Mean score and SD of the *Hit 3* scores as a function of age group

Age	40's	50's	60's	70's+
Male Mean	46.56	47.70	40.01	34.94
SD	14.26	9.21	12.35	10.03
Female Mean	53.38	46.88	39.06	33.37
SD	13.50	10.64	10.48	9.87

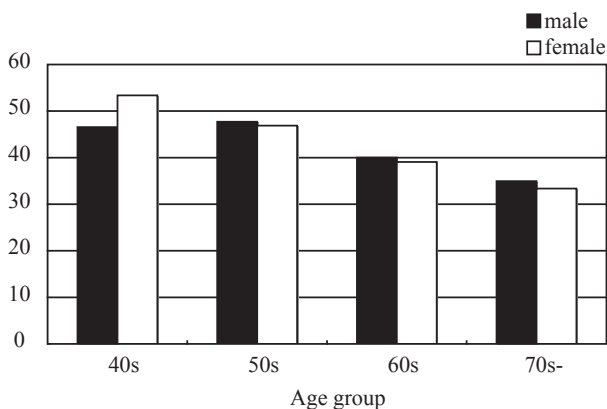


Figure 2: Sex difference in perceptual speed by *Hit 3*

group was better than that of 70's+ onward ($p < 0.001$). That is, the perceptual speed in cognitive demanding target inspection task decreased from the 40's age group. This study found sex difference only in the 40's age group ($p < 0.001$), whereas there was no significant sex difference in the other age groups (50's, $p < 0.69$; 60's, $p < 0.64$); and 70's+, $p < 0.44$, respectively).

3.3 Logical memory

Table 4 and Figure 3 show *logical memory* scores of male and female participants as a function of age group. The performance of the 40's age group was better than that of the 50's age group ($p < 0.001$), the 50's age group was better than that of 60's ($p < 0.001$), the 60's age group was better than that of 70's+ onwards ($p < 0.001$). That is, the logical memory performance decreased gradually from the 40's age group. This study found sex difference in logical memory performance showed up only in the 40's age group ($p < 0.001$), whereas there was no significant sex difference in the other age groups (50's, $p < 0.14$; 60's, $p < 0.44$); and 70's+, $p < 0.82$).

Table 4: Mean score and SD of the logical memory scores as a function of age group

Age	40's	50's	60's	70's+
Male Mean	13.30	11.67	10.15	8.37
SD	5.41	4.69	5.57	5.09
Female Mean	16.20	13.43	10.88	8.16
SD	5.43	5.02	4.70	4.28

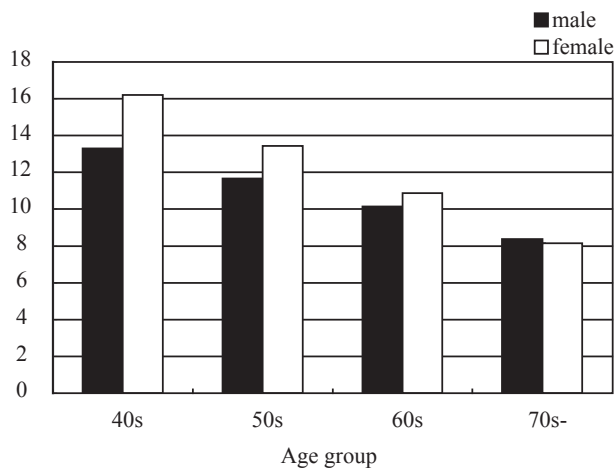


Figure 3: Sex difference in logical memory task

3.4 Letter fluency

Table 5 and Figure 4 show *letter fluency* scores of male and female participants on the D-CAT as a function of age group. The results were slightly different from the above three measures. The performance of the 40's age group was better than that of the 50's age group ($p < 0.001$), the 50's age group was better than that of the 60's age group ($p < 0.001$), whereas the

Table 5: Mean score and SD of the letter fluency test scores as a function of age group

Age	40's	50's	60's	70's+
Male Mean	26.26	20.93	17.92	17.87
SD	9.66	6.83	8.02	8.81
Female Mean	25.76	22.70	21.68	20.53
SD	7.87	8.31	7.13	7.27

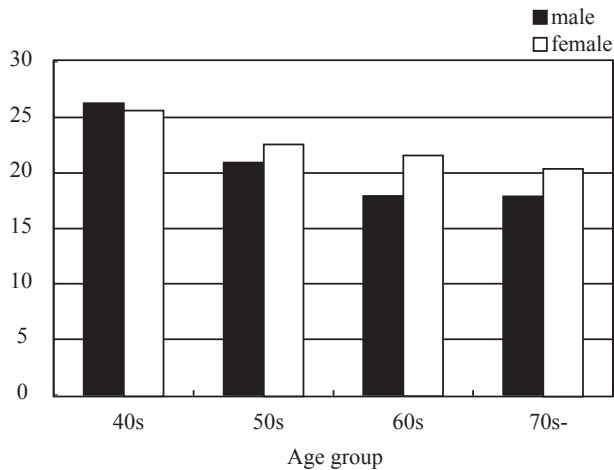


Figure 4: Sex difference in letter fluency task

60's and over the 70's+ age group was not different ($p < 0.54$). Hence, *letter fluency* performance decreased gradually from the 40's age group to the 60's age group, but it remained stable after 60's. The sex difference in letter fluency showed up only in the 60's age group ($p < 0.05$), whereas there was no significant sex difference in the other age groups (40's, $p < 0.73$; 50's, $p < 0.44$); and over 70's+ age group, $p < 0.16$, respectively).

4. Discussion

The purpose of this study was to examine sex-related developmental changes of perceptual speed (measured by the digit cancellation test), memory (measured by Wechsler's logical memory), and verbal fluency (measured by letter fluency test) in middle and old age people.

There are two reasons to conduct the present study. First, there is not much data related to sex difference in cognitive abilities in later human life stages. Second, we aimed to examine the validity of a recent hormonal model for sex differences in cognitive abilities proposed by Kimura (1999) by the examination of cognitive performance in middle and old age people.

Figure 1, 2, 3 and 4 showed performance changes in perceptual speed, memory and verbal fluency as a function of age.

As expected, performance levels decreased gradually as a function of age. It was robust in perceptual speed and memory activities. However, verbal fluency did show rather different performance changes. The performance in the two oldest age

groups was not different. These findings suggest that the age effect reflect different cognitive facets of abilities and it is not identical. This means that one aspect of cognitive ability deteriorates, while other aspect of cognitive ability still remains consistent for a while longer. More concretely, the findings showed that perceptual speed (or attention focusing and sustaining) and logical memory recall deteriorate faster than language generation as a function of age from the middle to old age.

There is ample evidence to suggest that neural components that relate to sustained attention (or working memory) and word retrieval; in other words, that relate to digit cancellation task, memory, and letter fluency test are different.

Therefore, our findings are not special. Actually, functional brain-imaging studies of intact adults have shown that the pre-frontal cortex is activated during the performance of sustained attention (e.g., Awh, et al., 1996; Fiez, et al., 1996; Paulesu, et al., 1993; Jonides, et al., 1993; Smith, et al., 1995). A fMRI study by Mead, Mayer, Bobholz, Woodley, Cunningham, Hammeke, and Rao (2002) also indicated that the component of selective attention in the test invites the activation of frontal cortex, especially around the area of BA44. Baldo, Shimamura, Delis, Kramer, and Caplan (2001) assessed word retrieving functions using the verbal and nonverbal fluency test on a group of patients with focal frontal lobe lesions and age matched healthy control participants. The results showed that participants with frontal lobe lesions were impaired, in comparison to the control participants on both verbal and nonverbal fluency tests. Participants with left frontal lesions performed worse than participants with right frontal lesions on this verbal fluency test, while the groups did not differ in the nonverbal fluency test. These reports indicate that neural components that relate to digit cancellation task, memory, and the letter fluency test are different.

A plausible reason why deterioration on word generation ability by aging is slower than that of the perceptual speed and logical memory abilities is not apparent at present. One possible candidate of interpretation for this discrepancy might relate to the neural process complexity that relates to task performance.

In the letter fluency task performance, at least, participants have to search for nouns, which begin with a given target letter (syllable) from the mental lexicon and they must try to avoid proper nouns from the candidates and words generated earlier, then they must generate a word (to prepare neural coordination for word articulation). In other words, to complete the letter fluency task, various parts of neural components have to work together. On the other hand, in the digit cancellation task and memory recall, process in performing both tasks seems to be less complex than that of the letter fluency task. Low vulnerability by aging or endurance in cognitive ability might be the reflection of the degree of complexity of neural networks that the cognitive task involves. When a cognitive ability consists of stronger synergistic work of complex neurological components, it must be tough and invulnerable for aging. This interpreta-

tion is based on the hypothesis that the healthy brain works in a solution-oriented way, that is, it works dynamically to seek the best solution (Hatta, 2003).

Another possible interpretation is that as the letter fluency task consists of plural processes, word search, proper noun inhibition, and word articulation, the arousal level of neural function to conduct cognitive tasks maintains a high level in old age people compared to the fact that digit finding and memory recall consists of simple process.

In short, a different deterioration curve among different cognitive abilities provide suggestions of how to keep proper communication with middle and old age people.

Figure 4 showed also that the performance level in the letter fluency decreased gradually from the 40's to the 60's age group but it remained constant after the age of 70 years old onwards. Since the finding seems to suggest the existence of rare elite survivor as Ribbitt proposed (Rabitt, Lowe, & Shilling, 2001). As majority of people over the age of 70 are hospitalized, bedridden, or in sheltered accommodation, they are unavailable for testing in a health examination by the community health care system. Therefore, it seems certain that the older samples who have been assessed in behavioral testing of cognitive ability in old age have been elite and atypical members of their age groups.

As for the second purpose, there has been a long debate on the issue of sex difference (or gender difference) in human cognitive abilities, whether women and men differ in terms of their intellectual abilities. Women are sometimes said to outperform men in verbal ability, and men are said to outperform women in mathematical and spatial ability. Some researchers still insist that much research on gender difference in cognition has been poorly conceived and executed and its findings have been quite irresponsibly interpreted in order to keep women in their place (e.g., Caplan & Caplan, 1997). They suggest that there are many profound conceptual and methodological problems that undermine the validity of research on gender difference in cognitive abilities.

However, more recently, Kimura (1999) reviewed studies that related to sex difference in various cognitive abilities from a wider viewpoint than that of Caplan and Caplan (1997) including neuropsychological studies. Her conclusion did not perfectly correspond with the general belief that females possess better verbal skills than males do. For example, females do not have larger vocabularies or higher verbal intelligence than males as has been considered, though females are better spellers and have better verbal fluency. Females perform consistently better than males on tasks of verbal memory. The most important point in her conclusion relates to a nature or nurture debate in sex difference of cognitive abilities. As for the reason of the sex difference in cognitive ability, she stressed the importance of the sex related hormone rather than cultural or environmental factors. She introduced the persons with early hormonal anomalies

such as congenital adrenal hyperplasia (CAH), idiopathic hypogonadotropic hypogonadism (IHH) and androgen insensitivity indicates early exposure to androgen contributes significantly to scores on various spatial tasks. As for verbal ability, she introduced evidence that fluctuations in estrogen levels are associated with changes in verbal fluency, perceptual speed and taking estrogen therapeutically enhance verbal memory on older females. Considering these conclusions, Kimura maintains that cognitive abilities are strongly influenced by early and/or current hormonal environments and socialization influences on sex difference in cognition is meagre. This invites an expectation that verbal ability of a sex and perceptual speed is not constant throughout human development. It is expected that the robust sex difference in verbal ability and perceptual speed will diminish in elderly people, more concretely, after the age around menopause in females. In this study, we addressed the validity of Kimura's proposal. The results in perceptual speed seemed to coincident with Kimura's proposal.

As seen from Figure 1 and 2, the *Hit 1* and *Hit 3* performances were very similar. In relation to sex difference, females' superiority was apparent in the 40's age group but diminished from the 50's age group and hereafter there was no difference between males and females. As the average life span of the Japanese woman has increased from 50 years to 82 years old for the last 70 years, the mean climacteric age remains unchanged, around 50 years old (Taketani & Maehara, 2001). The finding that female superiority diminished from the 50's age group seemed to correspond with the proposal by Kimura from the viewpoint of the mean age of climacteric of Japanese women. These results seem to support Kimura's hormonal interpretation of sex difference in cognitive ability and strongly suggest a possibility that the sex hormone such as estrogen suggests female-favoring cognitive ability.

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