Physiological Diagnosis and Rehabilitation for the Alzheimer Type Dementia

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Abstract. Light reflex and oculogyration analysing system is proposed in order to diagnose the Alzheimer type dementia (DAT) objectively. 19 patients are studied, which shows that the maximum miosis ratio and miosis velocity are sensitive parameters to evaluate the severity of dementia and the changing time of internal and external rectus eye muscles is the effective index for screening of the dementia. The threshold of the changing time over 0.35 second can discriminate DAT clearly from the normal. Biofeedback trainings of the demented are executed by the objective diagnosing method, which shows improvement in MMSE, ADL score and the eye reflex parameters. The proposed method may become a safe non-pharmacological treatment of the dementia.

Keywords: Alzheimer type dementia, physiological diagnosis, light reflex, eye pursuit, and rehabilitation.

1 Introduction

The number of Alzheimer dementia patients (AD) is supposed to become almost 5 million in Japan by 2030. As the aetiology is unknown, the early diagnosis is important in order to slow down the aggravation by donepezil and brain rehabilitations. The screening methods are not only subjective (MMSE, HDS-R etc.) but also time consuming (15∽45 minutes) in the early stage, when the brain imaging (CT, MRI or PET) is neither so effective nor decisive in this period.

We have found the abnormality of eye reflexes in Alzheimer dementia patients, that is rapid and objective and it can be widely used from the early to the final stage of dementia evaluation even in ordinary primary care settings.

As we believe that every medical diagnosis should contribute patients' cure and care, we have studied the effect of non-pharmacological treatment of the dementia by peripheral stimulations including electrical current or visible light with the new diagnosing systems. About 40% of the AD patients have revealed the improved MMSE scores in short period after the treatment.

In this study we try to apply the biofeedback training for self-cure by AD patients' themselves adding to the former electrical stimulations on acute points. The result is rather encouraging with the effect of 50%, so we hope that our proposed complex treating method might become a safe and self-cure even in the AD patients' homes.

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2 New Objective Diagnosing Methods

Scinto et al. found that the pupil midriatic time response by tropicamide in AD patients were abnormal [1-14, 19, 20]. But his method is not only unavailable especially for elders with glaucoma and also unstable and time consuming (about 1 hour). We have improved the shortcomings by using visible light stimulation instead of midriatic medicine and by measuring constricting speed (Fig.1) [15-18].

The original system has the following features.

- Light stimulation by small lamp
- Infrared CCD camera detected pupil image
- Automatically calculated diameter of the pupil by a personal computer.

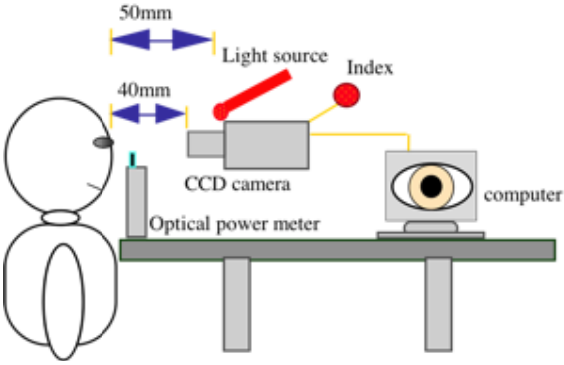

Fig. 1. Light reflex measuring system

We have found that the pupil constriction (= miosis) of the demented patient by visible light stimulation is less in the response size and slower than the normal elders (Fig.2) [21-23]. Several parameters are calculated from the light reflex curve (Fig.3). Maximum miosis ratio and 10%-90% Miosis velocity are most sensitive parameters to evaluate the severity of dementia.

The 83 clinically diagnosed demented patients and 32 normal elders are tested as the subjects for the system. Alzheimer type dementia (DAT) can be diagnosed by miosis rate (MR_{Max}) with $p < 0.05$ (Fig.4). All type of the dementia can be discriminated by the miotic time (Mt) with $p<0.05$ or 0.01 (Fig.5).

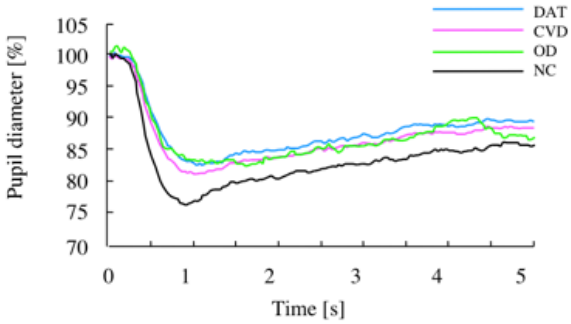

Fig. 2. Light reflex curves of the dementia (DAT: Alzheimer dementia, CVD: Cerebro-vascular dementia, OD: Dementia of other type, NC: Normal control)

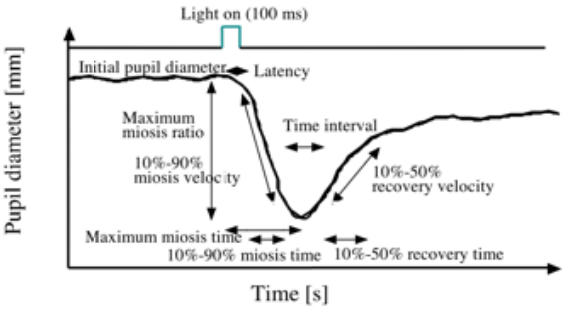

Fig. 3. Light reflex parameters

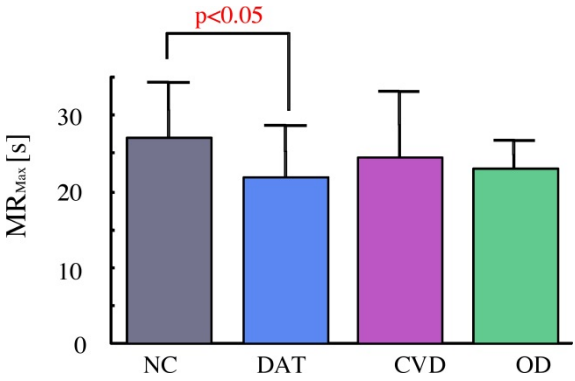

Fig. 4. The miotic rate (MR_{Max})

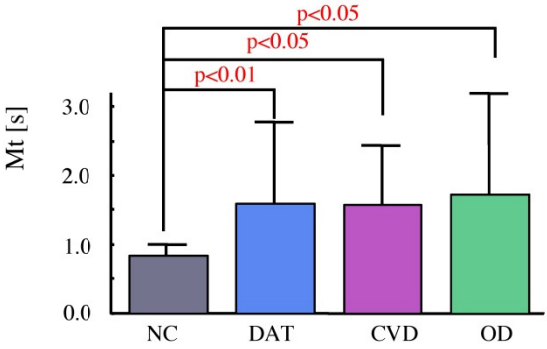

Fig. 5. The miotic time (Mt)

The two-group discriminant analysis of the light reflex (Table 1) shows sensitivity (88%), specificity (97%), positive correction probability (90%), and LR + (Likelihood ratio for a positive finding)[28].

The Three-Group discriminant analysis of the light reflex (Table.2) shows that good sensitivity (96%) and specificity (100%) for DAT while sensitivity (79%) and

specificity (97%) for CVD. The positive correction probability is 71% for DAT and 55% for CVD, while the overall (DAT + CVD) is 76%.

The LR + (Likelihood ratio for a positive finding) is ∞ for DAT and 25 for CVD.

The result of the light reflex is rather good comparing the other subjective diagnosing method, but the ppositive correction probability is estimated to be greater than 80% for ordinary screening of the dementia.

To improve the original system we add an eye tracking mechanism and construct an improved eye reflex and tracking-diagnosing units (Fig.6) [24-27].

Table 1. Two-group discriminant analysis

		Clinical Diagnosis	
	Subjects	Dementia	Control
Light Reflex	Dementia	73	1
	Normal	10	31

Table 2. Three-group discrimination analyses

		Clinical Diagnosis		
	Subjects	DAT	CVD	Control
Light Reflex	DAT	45	6	0
	CVD	16	11	1
	Normal	2	3	31

The subjects are 19 demented patients; AD (75.1±5.9 years old, HDS-R=11.3±7.7), 18 normal elders; EC (79.5±7.4 years old, HDS-R=27.9±3.4) and 7 healthy young volunteers; YC (24.9±4.8 years old, HDS-R=30.0). Subjects are instructed to wear a glass-type attachment that includes a small LCD monitor and a CCD digital camera. They are also instructed to track a small black dot running on a horizontal line in the LCD monitor from the right to left and vice versa randomly. The velocities of pursuing target are 300, 400 and 500 pixel/s. The location of an eye's pupil center is automatically calculated using cornea light reflex method by a built-in processing unit in the system through the CCD camera.

Each five measured data of three types of the subject are adjusted by initial values and are rendered to visible curves by summation-averaging method. The adopted summation-averaging technique could successfully eliminate randomly inserting saccade that used to be annoying noises for the detection of the smooth pursuit eye movement. The oculogyration responses are calculated from the pupil center data afterward and are visualized as simple time versus eye-location curves in an off line batch process of connected another desktop type personal computer. As diagnosing parameters, we have adopted the switching time of internal and external rectus muscles, velocities, peak values, the averaged difference between the patient and the normal.

The subject is instructed to follow a moving object from the left side to the right repetitively in the gaugle. The sweeping speeds are 300, 400 and 500 pixel/s. The eye-tracking image is measured by CCD camera installed in the same gaugle.

AD patients show the weaker and slower tracking curves than the normal elders. Especially the changing time of m. rectus lateralis and medialis seems to be the most sensitive parameter.

Fig. 6. The improved measuring unit with gaugle(Left)

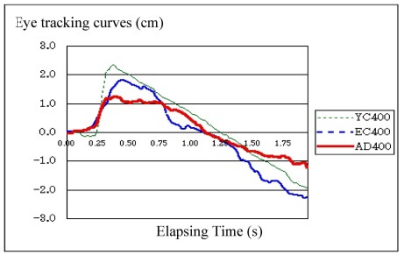

Fig. 7. An eye tracking curves (Right AD: Alzheimer, EC: normal elder, YC: normal young)

The relative peak value of the Alzheimer patient falls more sharply in AD patient than the normal elders and the normal young according to the object speed (Fig.8).

Especially the changing time between the outer and inner muscles has clear negative correlation (r = -0.72) with MMSE and all AD patients have the changing time of over 0.35s (Fig.9).

The two objective diagnosing methods with light reflex and eye tracking seem to be both effective and complementary in the dementia screening as well as the evaluation during treatment.

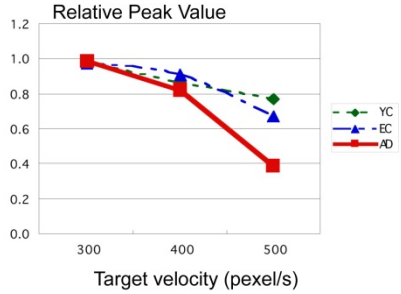

Fig. 8. Relative peak value by target velocity change. The 19 Alzheimer patients (AD), 18 normal elders (EC) and 7 normal young (YC) show clearly different eye-tracking parameters.

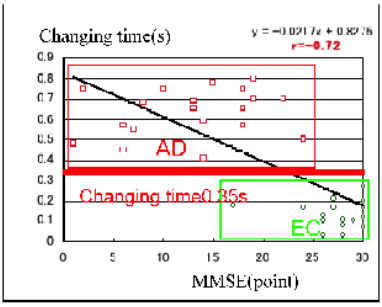

Fig. 9. The changing time of the outer and inner rectus muscles

3 Rehabilitation of the Dementia

As the aetiology and aggravation mechanism of dementia are both unknown, no fundamental treatment is developed by now. Only donepezil is used to retard the progression but the effect is restricted in about 0.5 to 2 years.

On the other hand it is said that only 10% of the 14 billion human neurons are used in his/her life and that neurons can be newly yielded in need. If the damaged neurons in the dementia are possible to re-activated or re-produced by outer stimulation, we believe that non-medical treatment should be realized.

We are studying the dementia improving effect with stimulating energy (mechanical, electrical and visual) on patients' peripheral nerves.

3.1 Mechanical Stimulation

In oriental medicine mechanical stimulation such as acupuncture (=Sinkyu) or finger pressure (=Shiatsu) is widely used for non-pharmacological treatment of diverse diseases. Especially they are effective for nervous system disorder (e.g.: neuralgia, paralysis, convulsions, stroke recovery, polio, insomnia), we assume it may be applicable to the dementia.

A commercial foot-sole patting machine is used for the mechanical stimulation on acute point KI01 (Yuusen) in 13 dementia patients (81.7±3.8years old). The treatment is executed for 15 minutes x 2 times a week during 1 month.

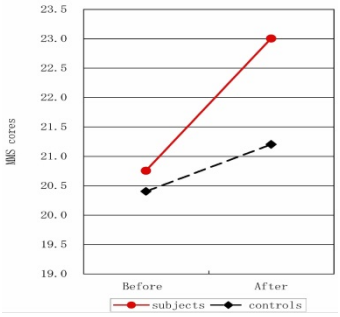

Fig. 10. Mechanical stimulation on foot sole

The averaged MMSE of the patient are improved from 20.8 to 23.0 (Fig.10).

The ADL of the patients is also improved especially in affective aspect. Is also improved especially in affective aspect and abnormal behaviours ($p<0.01$).

3.2 Electric Stimulation

TENS (transcutaneous electrical nerve stimulation) on acute points is also widely used as a variation of acupuncture. A commercial TENS apparatus (Trio300, 0.3∽400Hz, Burst wave 25mA) is applied to 11 dementia patients (5 mild and 6 severe, 75.6years old) for 30 min/day, 3 times/week for 1 month. Stimulating point is Seimei (BL1) that is an acute point for relief of headache and asthenopia (Fig.11).

HDS-R is improved from 10.3±5.0 to 14.3±6.2 in mild group and from 3.7±1.6 to 6.0±5.4 in severe group. SMT-7 and the light reflex parameters are also improved in all patients [28-30].

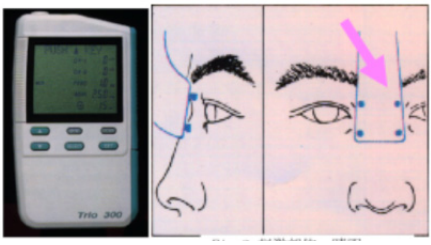

Fig. 11. TENS apparatus and acute point BL1

3.3 Light Stimulation

Light stimulation by LED in the gaugle (1s, 5 times/min., 3trials a day for 3days) is tried for 15 DAT patient (81.6 years old, 10 females) and 15 CVT patients (75.6 years old, 3 females). HDS-R scores of 3 AD and all 5 CVD patients are improved (Fig.12). The light reflex parameters are also improved (Fig.13).

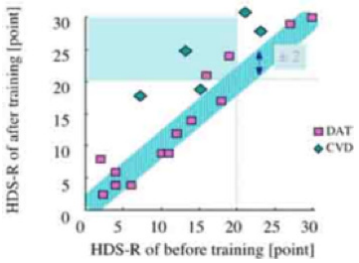

Fig. 12. HDS-R change by light stimulation

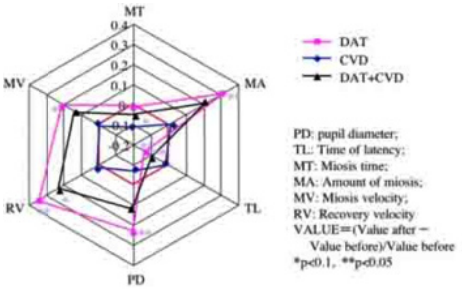

Fig. 13. Light reflex parameter change by light stimulation

3.4 Comparison of Peripheral Stimulation Effect

Comparing the three stimulating energy on the peripheral sensor, the light and the electric stimulation are more effective for dementia improvement than the mechanical one (Fig.14).

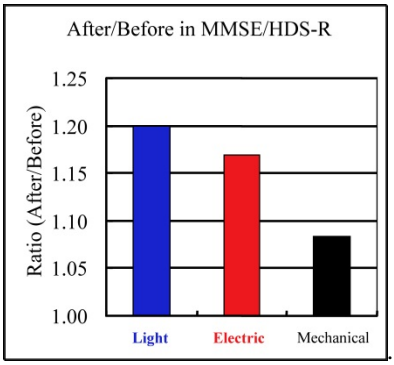

Fig. 14. Comparison of three types of stimulation

3.5 Biofeedback Rehabilitation

Expecting the better improving effect, we propose a new complex treatment by TENS and visual biofeedback. TENS on acute point BL-1 is used as peripheral nerve stimulation. At the same time the visual images of pupils are presented to the patients as biofeedback signals (Fig.15). Subjects are 4 Alzheimer dementia patients (3 females, 77.0±7.4 years old, HDS-R: 16.0±4.4 ; MMSE: 17.3±6.0).

Treatment is total 10 trials, each 30 min, every other day. The peripheral stimulation is given by TENS of the acute point "Seimei-ketsu"(BL1). The biofeedback signal is the visual images of patients' pupils. MMSE, HDS-R and 7 memorizing items are tested as the intellectual evaluators. The latency time, light reflex time, speed and the inner-outer straight muscle changing time is measured as the physiological evaluators. N-ADL scale and N-M scale are also done as the ADL evaluator.

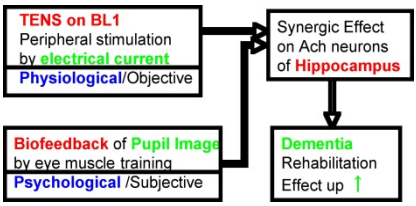

Fig. 15. Complex treatment by TENS and visual biofeedback

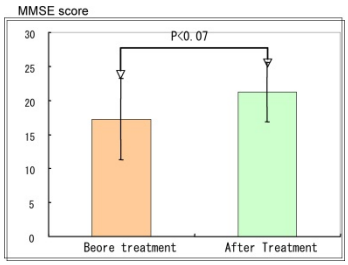

Fig. 16. MMSE improvement by complex treatment of TENS and the visual biofeedback

The results of the complex treatment show higher effect for improvement of the dementia in MMSE/HDS-R as well as the physiological parameters than the simple peripheral stimulations (Fig.16 & Fig.17).

The extended trial shows that the 10 out of the 20 Alzheimer patients are improved in HDS-R by the complex treatment. The complex treatment with biofeedback is more effective (50%) than the TENS only treatment (40%) even in the scaled up trial (Fig.18).

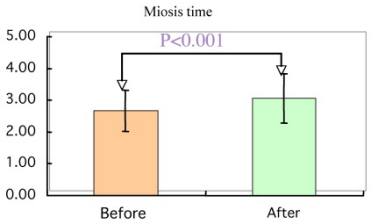

Fig. 17. Miotic time improvement by complex treatment

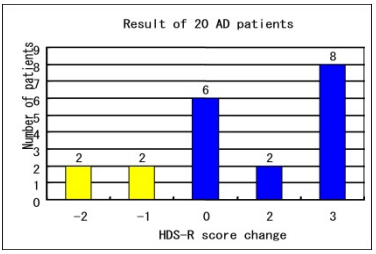

Fig. 18. Result of the extended trial

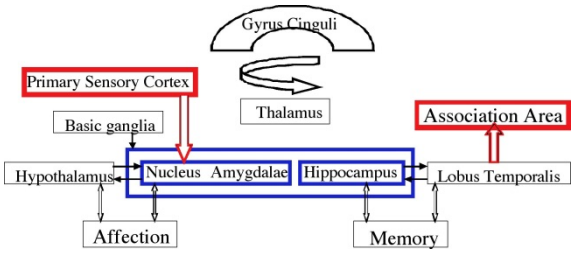

Fig. 19. A neural model of CNS modulation by peripheral stimulation

The peripheral sensory stimulation may modulate the signals from Hypothalamus to Lobus temporalis in Nucleus amygdalae / Hippocampus (Fig.19). The method might yield a new non-pharmacological arsenal for the treatment of dementia [23].

4 Conclusions

The light reflex and eye tracking parameters are adopted as the physiological evaluators for Alzheimer dementia. TENS on acute point BL-1 is used as peripheral nerve stimulation. At the same time the visual images of pupils are presented to the patients as biofeedback signals. The results of the complex treatment show higher effect for improvement of the dementia in MMSE/HDS-R as well as the physiological parameters than the simple peripheral stimulations. The method might yield new non-pharmacological arsenals for the treatment of dementia.

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