Quick Screening Mild Cognitive Impairment and Dementia using Quantitative Evaluation of Motor Control Function

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Abstract: The Visual synchronization task (VST) evaluates the motor control function, generates evaluation parameters, and takes only 25 seconds to complete. Evaluation parameters of the VST were tested as predictors of micro cognitive impairment (MCI) and dementia. The mean rotation speed parameter decreased in order of control, MCI, and dementia groups. With the mean rotation speed parameters of right hand in the first period (represented as AveP3rR1), p-value of t-test between the control group and the dementia group is 8.37×10^{-13}, and AUC is 0.863. Between the control and dementia groups with 0.765 as a cut-off value of the AveP3rR1, specificity is 0.84 and sensitivity is 0.77. Using the mean rotation speed of the right hand in the first period as the evaluating parameter, the VST can be measured in less than 15 seconds, which enables an easy screening for MCI.

Keywords: Dementia, Micro cognitive impairment (MCI), quick diagnosis, motor control function evaluation method, precise quantitative evaluation

1. Introduction

This study proposes probable parameters for screening of brain disorders including dementia and micro cognitive impairment (MCI) using the motor control function evaluation method called visual synchronization tasks (VST). Japan has an increasingly aging society, in which 28.1% of the population is composed of elderly people [1], [2]. Dementia is the most common age-related neurodegenerative disease and therefore, the health, social and economic impact resulting from dementia will continue to increase alongside the longevity of the population. The prevalence rate of dementia is estimated to be around 10% in the elderly people in Japan. Alzheimer's disease is most common cause of dementia and currently an irreversible process with treatments that only slow the progression of the condition [3].

Minimal mental state examination (MMSE) is the most commonly used scale for the detection of Alzheimer's disease and other dementia [4], while the VST evaluates many aspects of brain functions [5], [6], [7], [8], and is effective index for the development of brain function in elementary school students [9], [10], [11]. It has also been shown that the VST is an effective indicator of brain function decline in older people [12], [13].

This paper discusses the effects of MCI and dementia on motor control function measured by the VST [5]. The motor control function evaluation method is safe, simple, and non-invasive; it does not require special equipment that attaches to the patient's body and is conducted in 25 seconds in the seated position, without the requirement of global movements. The method is easy to complete. It needs only 25 seconds, and is performed in seated position. No global movements are needed.

In this paper, we will introduce the measurement method, patients, and control group construction. Then, the analysis and proper parameters to evaluate the effect of MCI and dementia will be reported and discussed using the experimental data. And last, the findings and impact of our findings will be highlighted.

2. Method

2.1 Measurement session

One measurement session was conducted to evaluate the effect of dementia is using the VST. The brain performance is evaluated and compared to the motor control function as part of the VST.

A VST can be completed in 25 S. **Fig. 1** shows the structure of a visual synchronization task. One VST is constructed in two stages. In the first stage, stimulus movement is displayed and in the second stage, no stimulus movement is displayed. The subject rotates their hands as the stimulus movement with and without displayed stimulus movement.

The proposed method enables the fast screening of the brain dysfunctions including MCI and the dementia. The VST can determine MCI probability at very low cost and

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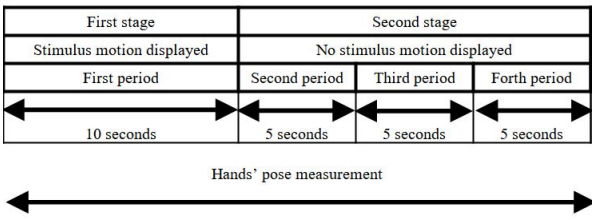

Fig. 1 Structure of the visual synchronization task (Relations between stimulus and analysis periods).

may be useful as an initial screen for MCI and dementia.

3. Basic measurement parameters

3.1 Evaluation parameters

At each stimulus cycle of the VST, non-smoothness measure (NSM), the phase of the participant's movement synchronized with the stimulus movement, and the power of the participant's movement synchronized with the stimulus movement were calculated. The Power of three cycles in ratio (P3r) was obtained at each of the three continuous stimulus cycles and was calculated as follows: The moving speed $P3r$ (Power of 3 cycles in Ratio) was defined as (1). $P3r$ is the power of stimulus in lower 3 components in ratio.

$$P3r = \frac{P3_3}{P3_1 + P3_2 + P3_3} \quad (1)$$

In (1), $P3_n$ represents the power of the $n/3$ Hz component at each of the three continuous stimulus cycles. When a participant follows the stimulus movement completely, there is no slower movements. $P3_1$ and $P3_2$ are zero and therefore, $P3r$ is 1.0.

3.2 Evaluation parameters at each period

The first and second stages together have a total of four periods. At each period, statistical parameters for NSM, the phase in which the participant's movement synchronized with the stimulus movement, and the power of the participant's movement synchronized with the stimulus movement, that are listed below.

- Mean
- Median
- Lower quartile
- Minimum
- Fluctuation range
- Standard deviation

Only the mean was calculated for P3r.

3.3 MCI and Dementia groups

VST trials were conducted with permission from the Utsunomiya University Ethical Council.

The participants of 100 VST trials had undergone the MMSE (Minimal Mental State Examination). The participants with MMSE total under 28 and over 23 were included in the MCI group. Those with MMSE scores equal or under 23 were included in the dementia group.

The MCI group included 30 VST trials and 6 participants. The mean age of the participants included in the trials was 71.2 years old.

The dementia group included 70 trials and 21 participants. The mean age of the participants in these trials was 83.8 years old.

3.4 Control population

From the VST participants, those within normal limits, with only high blood pressure, and Hyperlipidemia were selected as the candidate control group, which included 763 VST trials and 172 participants. From their medical records, about 60% of the subjects had no neurological problems and therefore, were selected as healthy subjects.

3.4.1 Age

Motor control function degrades with the aging process [12], [13]. The candidate control group included more relatively young people than the MCI group. To compensate the difference in age, the participants under 58 years old were removed from the candidate control group, resulting candidate control group included 374 trials. The group's average age was 71.5 years old, which was similar to the mean ages of the MCI group and included 143 participants. The number of within normal limit (WNL) participants was 15 and included 47 trials. The number of high blood pressure participants was 90 and included 240 trials. There were 38 Hyperlipidemia participants who comprised 87 trials.

3.4.2 Difference of rotation between both hands

Healthy peoples have no difficulties rotating their hands in stimulus 1 Hz supination/pronation movements, with both hands synchronized. In healthy peoples, the differences in the movements between both hands are small and therefore, the large differences between the rotations of both hands indicates problems with the measurements or the executions of the trials. Outliers were removed based on the movement differences between hands. Differences in the rotation powers synchronizing the 1 Hz stimulus movements (represented $P3_3$ in (1)) between hands in the first period are shown in the left panel of **Fig. 2**. In a box plot of this paper, the box is drawn from Q1(first quartile) to Q3(third quartile) with a horizontal line drawn in the middle to denote the median. The whiskers extend to the most extreme data point which is no more than 1.5 times the inter quartile range from the box.

In the candidate control group, the trials out 3σ from the median were removed. This process was repeated until the group was fixed, resulting in 335 trials and 140 participants.

The standard derivation of the differences in rotation powers between both hands in the first period of the resulting candidate control group was 1159.4, with a mean of 438.7.

The same steps were repeated in the second and third periods, resulting in 300 trials and 132 participants. The standard derivation of the differences of rotation speeds of both hands in the first period of the resulting candidate control group was 1427.0, with mean of 626.6 and a median of 380.1. The differences of the rotation powers in the first period distribution is shown in the right panel of Fig. 2.

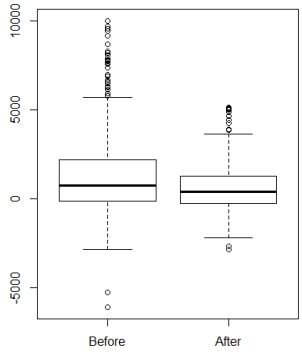

Fig. 2 The change of the distributions of the differences of rotation powers between hands in the first period in 341 pairs of a candidate control group and the distributions after the processing.
(The candidate control group before the processing is on the left, and the one after the processing is on the right.)

The average ages of the candidate control group was 71.5 years old and the number of WNL participants was 14 and included 39 trials. The number of participants with high blood pressure was 84 and included 199 trials, while there were 34 participants with hyperlipidemia, who participated in 62 trials.

3.4.3 Outliers removals for mean P3r of the right hand in the first period

Health people able to rotate their hands in a synchronized manner to stimulus images. In these cases, the mean P3r of the right hand in the first period (AveP3rR1) represented the speed of rotations based on the stimulus rotations and was kept relatively high. The mean AveP3rR1 of the candidate control group was 0.783, with a standard derivation is 0.139.

The candidate control group included some outliers; therefore, the candidate control group was reduced with AveP3rR1. The number of pairs in the candidate control group was 270, with a mean of 0.82 and a standard derivation of 0.086.

3.4.4 Outliers removals for mean NSM of the right hand in the first period

With the stimulus images, healthy peoples enables to rotate their hands synchronizing the stimulus images. In these cases, the NSM (non smoothness measure) that represents the degree of non-synchronization with the stimulus rotations and was relatively low.

The mean was 0.464 and had a standard derivation of 0.103.

To remove outliers from the group, the candidate control group was reduced so that it had a mean NSM to that of the first period. The number of trials in the resulting group was 251, which included 122 participants.

3.4.5 Outliers removals for mean P3r of the right hand in the first period again

With the stimulus images, healthy peoples enables to rotate their hands synchronizing the stimulus images. In the cases, the AveP3rR1 are kept relatively high. In the first period of the VST, a stimulus image is proposed.

Some outliers were left in the candidate control group. Therefore, the candidate control group was reduced as the previous step with the mean of P3rs in the first period.

The statistical values before the processing are listed below. The mean was 0.830. The standard derivation is 0.076. Apparently the group included some outliers.

The statistical values after the processing are listed below. The number trials was 244.The number of participants was 121. The mean of the mean of P3rs of the first period of the group was 0.836. The standard derivation was 0.069.

The candidate control group included 300 trials and 244 trials after processing. About 19% of the initial trials in the candidate control group were removed and reveals a ratio that was smaller than the 40% that were estimated from the daily clinical study. We used this reduced candidate control group for all further analyses.

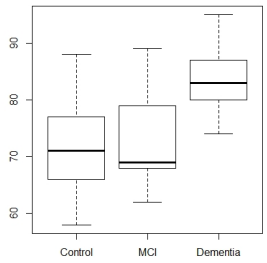

Fig. 3 The distributions of ages in the control, MCI, and dementia groups.

The distributions of the ages of the groups are shown in **Fig. 3**. The age distributions both of the control and MCI groups were nearly same while that of the dementia group was older than the control and MCI groups.

4. Screening parameters for MCI detection

The boundary between healthy individuals and those with MCI is not clear. The screening target population consisted of healthy individuals, MCIs, and dementias. Even if a screening method had enough power to identify probable MCI, if it overlooks dementia is not reliable. Therefore, we aimed to develop parameters could detect dementia with high probability and screen for probable MCI from healthy peoples.

4.1 Parameter evaluation criteria

121 valid healthy participants and 21 valid dementia participants were used for statistical analysis. However, six valid MCI participants were not enough for simple statistical evaluation. Therefore, between the healthy and dementia groups, the statistical differences were evaluated using a T-test and ROC (receiver operating characteristic) analysis. The distribution status of the control and test groups were visualized using a box plot.

Between healthy group and dementia group, p-value and AUC (area under curve) used as indicators of screening

power. Among the healthy, MCI, and dementia groups, the gradual distribution changes reflected the stability of the results, which indicated using a box plot.

4.2 Candidate parameter selection

The AUC and p-value of all parameters between the control and the dementia groups are listed in **Table 1**. They are plotted in **Fig. 4**.

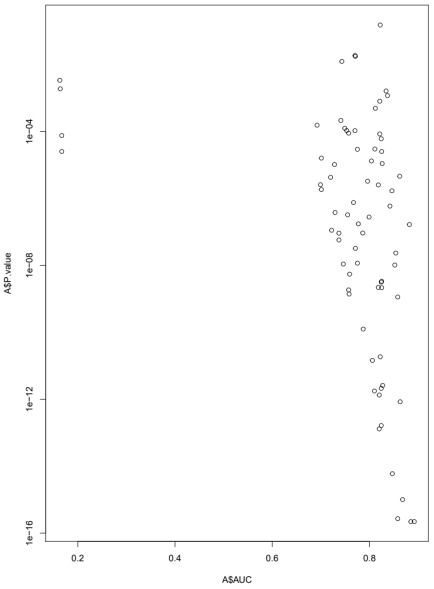

Fig. 4 AUC and p-values between the control and the dementia groups.

In Table 1, the first three characters represent the type of statistics. "Ave" represents the mean in a period, "min" indicates the minimum in a period. The difference and standard derivation of the results are indicated by "Dif" and "Qua", respectively.

The second three characters represent the type of parameter, including the non-smoothness measure (NSM), rotation power synchronized with the stimulus movement (PWP), the rotation speed defined by formula (1) (P3r), and the rotation power synchronized with three continuous stimulus movement cycles (P3P).

The last two characters represent left(L) or right(R) hand, while the first, second, third, and fourth periods are indicated with 1, 2, 3, or 4, respectively.

The p-value and the AUC were inversely correlated with one another (Fig. 4). From the distribution, the parameters that had p-values that were smaller than $1e-10$ and an AUC that was larger than 0.85 were examined in detail.

The selected parameters included AveP3rL2, AveP3rL3, AveP3rR2, AveP3rL1, and AveP3rR1, which represented the rotation speed in the first, second, and third periods.

4.3 Discussions based on The distributions of healthy, MCI, and dementia groups

Fig. 5 shows a box diagram of the means of the rotation

Table 1 AUCs and p-values of a t-test between the control group and dementia group and AUCs of the MCI group.

Parameter	Dementia-AUC	Dementia p-value	MCI-AUC
AveP3rL2	0.885	2.2×10^{-16}	0.735
AveP3rL3	0.892	2.2×10^{-16}	0.730
AveP3rR2	0.858	2.7×10^{-16}	0.683
AveP3rL1	0.868	1.0×10^{-15}	0.718
AveP3rR3	0.847	5.9×10^{-15}	0.688
AveP3PL3	0.820	1.3×10^{-13}	0.599
AveP3PR3	0.824	1.6×10^{-13}	0.544
AveP3rR1	0.863	8.4×10^{-13}	0.802
AveP3PL2	0.820	1.3×10^{-12}	0.601
minPWPL1	0.810	1.8×10^{-12}	0.633
AveP3PR2	0.824	2.1×10^{-12}	0.518
minPWPR1	0.827	2.6×10^{-12}	0.624
AveP3PL1	0.806	1.4×10^{-11}	0.606
AveP3PR1	0.822	1.9×10^{-11}	0.605
minPWPR2	0.787	1.2×10^{-10}	0.507
DifPWPL1	0.858	1.1×10^{-09}	0.704
AvePWPR1	0.758	1.4×10^{-09}	0.514
StdPWPL1	0.856	1.8×10^{-09}	0.703
minPWPL2	0.757	1.8×10^{-09}	0.550
DifPWPR1	0.825	2.1×10^{-09}	0.747
DifPWPR2	0.818	2.2×10^{-09}	0.620
StdPWPR1	0.824	3.2×10^{-09}	0.752
StdPWPR2	0.825	3.3×10^{-09}	0.621
AvePWPR3	0.759	5.5×10^{-09}	0.548
QuaNSMR1	0.852	1.0×10^{-08}	0.809
QuaPWPR1	0.746	1.1×10^{-08}	0.503
AvePWPR2	0.775	1.2×10^{-08}	0.483
MedNSMR1	0.854	2.3×10^{-08}	0.844
QuaPWPR2	0.771	3.2×10^{-08}	0.463
QuaPWPL1	0.737	5.7×10^{-08}	0.506
QuaPWPL2	0.737	9.2×10^{-08}	0.430
StdPWPL2	0.786	9.2×10^{-08}	0.718
MedPWPR1	0.722	1.1×10^{-07}	0.477
AveNSMR1	0.882	1.6×10^{-07}	0.856
DifPWPL2	0.777	1.7×10^{-07}	0.719
QuaNSMR3	0.799	2.8×10^{-07}	0.654
minNSMR3	0.755	3.2×10^{-07}	0.645
AvePWPL2	0.729	3.8×10^{-07}	0.544
QuaNSML1	0.842	5.9×10^{-07}	0.792
minNSMR1	0.767	7.5×10^{-07}	0.744
MedNSML1	0.846	1.7×10^{-06}	0.791
AvePWPL1	0.701	1.8×10^{-06}	0.545
AveNSML2	0.818	2.5×10^{-06}	0.703
MedPWPL1	0.699	2.6×10^{-06}	0.530
MedNSMR2	0.796	3.3×10^{-06}	0.710
MedPWPR2	0.720	4.3×10^{-06}	0.447
AveNSML1	0.862	4.6×10^{-06}	0.760
minNSMR2	0.728	1.0×10^{-05}	0.670
DifNSML1	0.826	1.1×10^{-05}	0.725
MedNSML2	0.804	1.3×10^{-05}	0.706
MedPWPL2	0.701	1.6×10^{-05}	0.608
StdNSML1	0.825	2.5×10^{-05}	0.725
AveP3rL4	0.167	2.5×10^{-05}	0.166
minNSML1	0.775	2.9×10^{-05}	0.746
StdNSMR2	0.811	3.0×10^{-05}	0.662
DifNSML2	0.824	6.1×10^{-05}	0.697
AveP3PL4	0.167	7.6×10^{-05}	0.156
StdNSML2	0.821	8.4×10^{-05}	0.701
AveNSMR2	0.757	8.9×10^{-05}	0.856
QuaNSMR2	0.770	1.1×10^{-04}	0.673
MedNSMR2	0.753	1.1×10^{-04}	0.844
QuaNSMR2	0.749	1.2×10^{-04}	0.809
minNSML2	0.692	1.5×10^{-04}	0.709
QuaNSML2	0.741	2.1×10^{-04}	0.689
MedNSMR3	0.812	4.9×10^{-04}	0.640
AveNSMR3	0.821	8.0×10^{-04}	0.656
DifNSMR1	0.837	1.2×10^{-03}	0.856
StdNSMR1	0.834	1.6×10^{-03}	0.856
AveP3rR4	0.164	1.9×10^{-03}	0.159
AveP3PR4	0.163	3.4×10^{-03}	0.157
AveNSMR4	0.743	1.2×10^{-02}	0.650
StdNSMR3	0.771	1.8×10^{-02}	0.651
DifNSMR3	0.770	1.9×10^{-02}	0.656
AveNSMR2	0.822	1.5×10^{-01}	0.683

Table 2 ROC analysis among the control, MCI, and dementia groups.

Cutoff value	Cont. spec.	MCI sens.	Dementia sens.	MCI +Cont.	Dementia +Cont.
0.733	0.873	0.500	0.700	1.373	1.573
0.734	0.869	0.500	0.700	1.369	1.569
0.737	0.865	0.500	0.700	1.365	1.565
0.741	0.865	0.500	0.714	1.365	1.579
0.742	0.865	0.500	0.729	1.365	1.593
0.744	0.857	0.500	0.729	1.357	1.585
0.748	0.852	0.500	0.729	1.352	1.581
0.749	0.848	0.500	0.743	1.348	1.591
0.756	0.844	0.500	0.743	1.344	1.587
0.757	0.844	0.500	0.757	1.344	1.601
0.765	0.844	0.500	0.771	1.344	**1.616**
0.768	0.840	0.500	0.771	1.340	1.612
0.769	0.840	0.533	0.771	1.373	1.612
0.774	0.836	0.533	0.771	1.369	1.607
0.775	0.832	0.533	0.771	1.365	1.603
0.778	0.828	0.533	0.771	1.361	1.599
0.779	0.824	0.533	0.771	1.357	1.595
0.782	0.824	0.533	0.786	1.357	1.609
0.785	0.820	0.533	0.786	1.353	1.605
0.786	0.816	0.533	0.786	1.349	1.601
0.787	0.816	0.567	0.786	1.382	1.601
0.788	0.811	0.567	0.786	1.378	1.597
0.792	0.807	0.567	0.786	1.374	1.593
0.795	0.807	0.600	0.786	1.407	1.593
0.797	0.803	0.600	0.786	1.403	1.589

speed measurements of the right hand in the first period of the control, MCI, and dementia groups, while those from the second and third periods are presented in **Fig. 6** and **Fig. 7**, respectively.

Healthy and MCI, and MCI and dementia are adjacent concepts, and their pathological conditions change continuously. Therefore, for screening probable MCI participants from healthy peoples, the gradual parameter change from healthy, MCI, and dementia groups respectively, was preferable.

Fig. 5, Fig. 6, and Fig. 7, overlap between the control and MCI groups increased, respectively, indicating that the mean rotation speed measurements of the right hand in the first period was most preferred. Other selected parameters may be better than AveP3rR1; however, for screening MCI and dementia from healthy people in the fourth period of the VST did not fit. Therefore, to screen for MCI and dementia, the fourth period of the VST should be omitted, suggesting that the VST can be shortened into 20-s trials.

4.4 Behavior of AveP3rR1

With the mean rotation speed measurement of the right hand in the first period, ROC between the control and dementia groups were calculated (**Fig. 8**). The AUC of the ROC was 0.86. **Table 2** shows the relationship among the cut-off values for the control, MCI, and dementia groups, indicating the best value for MCI and dementia identification.

Using 0.765 as a cut-off value, the specificity was 0.84 and the sensitivity was 0.77. The sum of the specificity of the control group and the sensitivity of the dementia group was 1.62. Around the 0.765 of the cut-off value, the sums of the specificity of the control group and the sensitivity of the dementia group remained large.

The ROC between the control and MCI groups are shown with respect to the mean rotation speed measurement of the right hand in the first period (**Fig. 9**). AUC of the ROC was 0.802, with a cut-off value of 0.765, a specificity was 0.84 and a sensitivity was 0.77. The sum of the specificity of the control group and the sensitivity of the dementia group was 1.62.

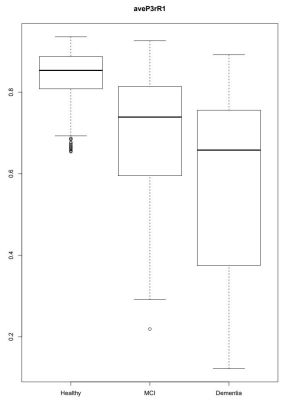

Fig. 5 Mean of the rotation speed measures represented by P3r of the control, the MCI and the dementia groups in the first period.

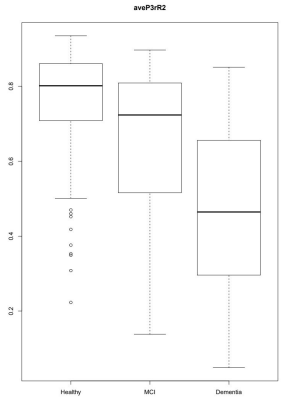

Fig. 6 Mean of the rotation speed measures represented by P3r of the control, the MCI and the dementia groups in the second period.

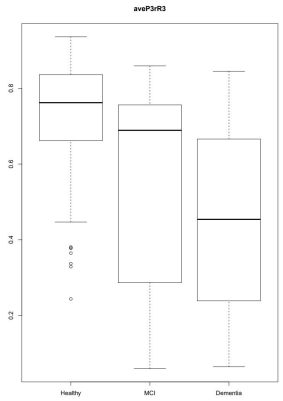

Fig. 7 Mean of the rotation speed measures represented by P3r of the control, the MCI and the dementia groups in the third period.

The control and MCI groups were adjacent, and their boundaries were not clear.

Using the mean rotation speed measurement of the right hand in the first period, VST trial can be shortened to less than 15 seconds in the first and second periods, which makes the VST trials easier to administer.

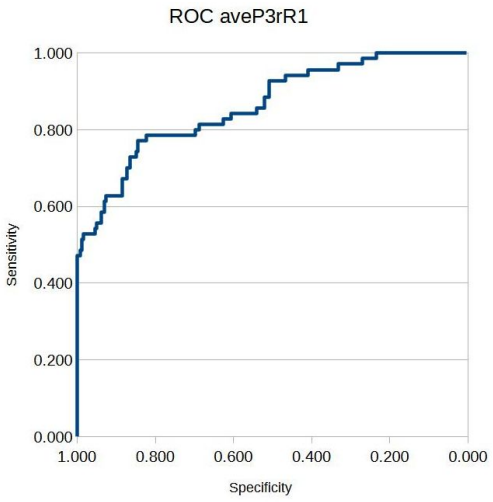

Fig. 8 ROC analysis comparing the control and dementia groups for AveP3rR1.

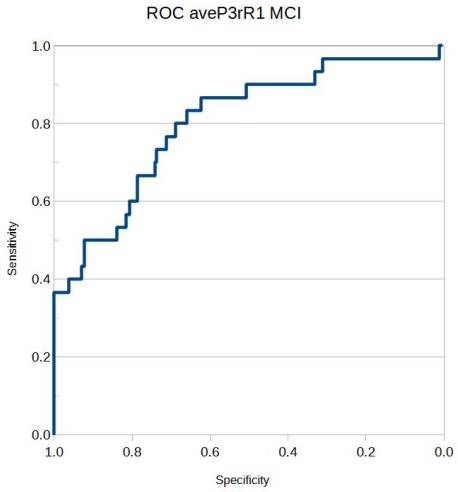

Fig. 9 ROC analysis comparing the control and MCI groups for AveP3rR1.

5. Conclusion

This study proposes effective parameters for screening for MCI and dementia from healthy people using the VST. The rotation speed parameters in the first, second, and third periods were effective at identifying MCI and dementia from healthy controls. Of the parameters, the rotation speed in the first period was the most effective at identifying MCI and dementia in this study.

However, the number of participants in the MCI group was only seven; therefore, large scale experiments are needed to clarify the detailed characteristics of parameters for screening for probable MCI in healthy cohorts. The number of participants of dementia was 26 , while the number of healthy participants was 199. These are large enough to statistical analysis and therefore, the effective parameters would work for screening MCI and dementia from a healthy population.

The VST took only 15 seconds, which is enough to measure effective parameters in the first period for screening for probable MCI cases when compared with the healthy group. This optimized VST is safe, not addictive, and easy to complete, making it an excellent tool for easily screening for MCI among otherwise healthy individuals.

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