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Assessment of the recovery of dynamic balance after intravenous sedation with midazolam

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Abstract
Purpose. To assess street fitness after sedation, computerized dynamic posturography (CDP) involving movement of the center of gravity may be more accurate than the conventional computerized static posturography (CSP). The purpose of this study was to evaluate the recovery of dynamic balance function after intravenous sedation by CDP in comparison with CSP, and to find a simple dynamic balance test that is well correlated with CDP.
Methods. The subjects were 20 male volunteers aged 20–27 years. After intravenous injection of midazolam ($0.07\,mg \cdot kg^{-1}$), four balance tests were performed. The recovery time and the percentage of subjects showing recovery (difference from the baseline value ≤10%) were compared. As CDP, a test in which unexpected perturbation stimuli are given using an unstable platform was performed. As CSP, standing sway tests were performed. Maximum speed walking (MSW) and usual speed walking (USW) tests were performed as simple balance tests.
Results. The recovery time in CDP (80 min) was longer than that in CSP (40–60 min). The percentage of subjects showing recovery in CDP (20%) was significantly lower than that in CSP (55%–70%) 60 min after the administration of midazolam. There was a significant positive correlation between the CDP test and the MSW test ($r = 0.67$).
Conclusion. CDP with perturbation stimuli detects the balance inhibitory effects of midazolam with greater sensitivity than CSP. The MSW test is well correlated with CDP with perturbation stimuli.

Key words Conscious sedation · Midazolam · Recovery of function · Dynamic balance

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Introduction

To assess the recovery of balance function after general anesthesia or intravenous sedation, Romberg's test or the linear walking test has been frequently used in clinical practice [1–3]. However, some studies have suggested low reliability of both tests [4,5]. Therefore, studies by computerized static posturography (CSP) have been performed to assess balance function more objectively and precisely [4–6]. Although computerized dynamic posturography (CDP) with movement of the center of gravity is more appropriate than CSP to determine whether safe discharge by walking is possible, there have been only a few studies that evaluated the recovery process of dynamic balance by CDP in comparison with CSP [7–9], and there have been no studies in which detailed evaluation was performed at short intervals. The application of CDP to daily clinical practice may be difficult due to economic considerations and the long duration of the test. Therefore, if a simple dynamic balance test that is well correlated with CPD can be introduced, it may be useful in clinical practice.

To evaluate the usefulness of the dynamic balance test, we observed the process of recovery of postural control ability after midazolam intravenous sedation using CDP with perturbation stimuli at 20-min intervals, and the result was compared with that assessed by CSP. In addition, the possible correlation between CDP with perturbation stimuli and two simple dynamic balance tests was evaluated.

Subjects and methods

After the approval of the ethics committee of our institution and informed consent had been obtained, 20 healthy male volunteers were enrolled in this study. Midazolam was administered in divided small doses over 4–5 min (total, about 0.07 mg · kg^{-1}) until the Wilson sedation score reached 3 (the eyes are closed, but the subject responds to one or two calls) [10]. Four balance tests were performed before administration of midazolam (baseline) as well as 40, 60, 80, 100, and 120 min after administration. As CDP, the dynamic balance test in which balance maintenance ability against unpredictable perturbation stimuli is assessed, was performed using a Stability System (Biodex Medical, Shirly, NY, USA). An unstable platform tilts in all directions according to changes in body weight applied to the tip of the toes and heels. The platform stability can be adjusted from level 8, which is the most stable, to level 1, the most unstable level. After our preliminary study, we used level 5 as a moderate and safe level in this study. The subjects were asked to keep the platform horizontal for 20 s. The index of the degrees of platform tilting in all directions from the horizontal line during the test was expressed as the stability index. As CSP, static stance sway tests were performed using a Balance Master System (NeuroCom International, Clackamas, OR, USA) by the previously reported method [6]. Static stance sway in the standing position was observed under three conditions (with eyes open, with eyes closed, and with visual feedback that allows minor adjustments of the position of the center of gravity). As simple dynamic balance tests, the usual speed walking (USW) test and the maximum speed walking (MSW) test were performed. The time required to walk 10 m at the maximum speed or the usual speed was measured [11]. For all measurement values, an increase indicates an increase in instability.

The recovery time was defined as the time until the significant difference between the mean value at each time point and the baseline value disappeared. It was analyzed by Friedman's test, and subsequent multiple comparison was performed by the Wilcoxon *t*-test with Bonferroni correction. The percentage of subjects showing recovery (difference from the baseline value ≤10%) was calculated at each time point. Comparison of the percentage of subjects showing recovery among tests was performed by the chi-square test, and subsequent multiple comparison was performed by Ryan's method. The relationship between the CDP and walking tests with the change from the baseline value was assessed by Spearman's rank correlation coefficient. $P < 0.05$ was considered to be significant. Values were expressed as the mean ± standard deviation.

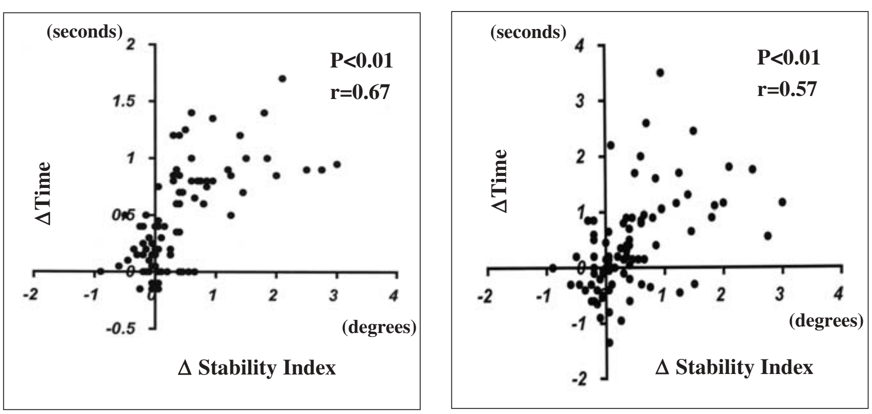
Results

The mean age, height, body weight, and body mass index in the subjects were 23.1 ± 2.0 years (range, 20–27 years), 171.1 ± 6.2 cm (range, 164–184 cm), 64.7 ± 8.2 kg (range, 53–85 kg), and 22.0 ± 2.6 kg · m^{-2} (range, 19–29.1 kg · m^{-2}), respectively. The mean administration dose of midazolam was 0.068 ± 0.006 mg · kg^{-1} (range, 0.053–0.074 mg · kg^{-1}).

Serial changes in values of CDP, CSP, and walking tests are shown in Table 1. The balance recovery times in the dynamic balance test, static stance sway tests, and walking tests were 80, 40–60, and 80 min, respectively.

Serial changes in the percentage of subjects showing recovery in each test are shown in Table 2. The percentage of subjects showing recovery in the dynamic balance test (20%) was significantly lower than the percentage of subjects showing recovery in the static stance sway tests (55%–70%) 60 min after the administration of midazolam.

There was a significant positive correlation between the results of the dynamic balance test and the walking tests ($P < 0.01$, $r = 0.67$ in MSW test, $r = 0.57$ in USW test) (Fig. 1).



Dynamic balance test vs **MSW test**

Dynamic balance test vs **USW test**

Fig. 1. Correlation between dynamic balance test and walking tests. There was a relatively high correlation between the dynamic balance test and the MSW test. *MSW*, maximum speed walking; *USW*, usual speed walking

Table 1. Serial changes in values of CDP, CSP, and walking tests after administration of midazolam (mean ± SD; $n = 20$)

Test	Measure (unit)	Baseline	40 min after	60 min after	80 min after	100 min after	120 min after	Recovery time
CDP								
Dynamic balance test	Stability index (°)	1.61 ± 0.42	3.38 ± 1.48**	2.27 ± 0.83**	1.74 ± 0.53	1.56 ± 0.37	1.51 ± 0.35	80 min
CSP								
Static stance sway tests	Eyes open sway (%)	0.045 ± 0.014	0.114 ± 0.102**	0.056 ± 0.036	0.058 ± 0.050	0.040 ± 0.038	0.039 ± 0.024	60 min
	Eyes closed sway (%)	0.059 ± 0.032	0.146 ± 0.092**	0.082 ± 0.075	0.070 ± 0.042	0.073 ± 0.055	0.068 ± 0.043	60 min
	Visual feedback sway (%)	0.035 ± 0.015	0.063 ± 0.042	0.052 ± 0.037	0.035 ± 0.019	0.037 ± 0.022	0.038 ± 0.022	40 min
Walking tests								
MSW test	Time (s)	4.75 ± 0.51	5.74 ± 0.75**	5.43 ± 0.70**	5.12 ± 0.60	4.87 ± 0.54	4.86 ± 0.54	80 min
USW test	Time (s)	6.94 ± 0.73	8.29 ± 0.96**	7.47 ± 0.73**	6.94 ± 0.63	6.63 ± 0.56	6.67 ± 0.57	80 min

CDP, computerized dynamic posturography; CSP, computerized static posturography; MSW, maximum speed walking; USW, usual speed walking
** $P < 0.01$(vs baseline)

Table 2. Serial changes in the percentage of subjects showing recovery

Test	Measure	Baseline	40 min after	60 min after	80 min after	100 min after	120 min after
CDP							
Dynamaic balance test	Stability index	100	0	20	50	95	100
CSP							
Static stance sway tests	Eyes open sway	100	10	65**	70	95	95
	Eyes closed sway	100	15	55*	70	75	75
	Visual feedback sway	100	35*	70**	80	95	95
Walking tests							
MSW test	Time	100	0	30	60	100	100
USW test	Time	100	20	40	90*	100	100

CDP, computerized dynamic posturography; CSP, computerized static posturography; MSW, maximum speed walking; USW, usual speed walking
* $P < 0.05$; ** $P < 0.01$ (vs dynamic balance test)

Discussion

CDP using the perturbation stimuli is subclassified into the platform sway or tilting load test with unpredictable random mechanical perturbation stimuli (mechanical perturbation test) and the test with stimuli perturbing visual, vestibular, or somatic sensation (sensation perturbation test).

Gupta et al. [7] performed intravenous sedation with $0.1\,mg \cdot kg^{-1}$ midazolam in adult volunteers and found a delay in the recovery time of dynamic balance function in the sensation perturbation tests (105 min) compared with that in static balance function (45 min). Ledin et al. [8] also performed intravenous sedation with $0.1\,mg \cdot kg^{-1}$ midazolam in adult volunteers and reported a delay in the recovery of sway velocity in the mechanical perturbation test (120 min) compared with that in static balance function (60 min). In our study, the dynamic balance test using an unstable platform [12,13] was performed as a mechanical perturbation test, and the recovery of dynamic balance function (recovery time, 80 min) was slower than that of static balance function (40–60 min). These results suggest that CDP with perturbation stimuli is a useful balance assessment test with high detection ability in terms of safe discharge by walking after intravenous sedation. Commissaris et al. [14] reported that multidirectional perturbations are desirable CDP condition because falls may occur in any direction in daily life, and habituation to the stimuli should be prevented. Other CDP conditions they described included loading appropriate for each subject. The CDP performed in this study as a perturbation test fulfilled all the above conditions. To obtain reliable data, subjects should become used to the measurement method. Concerning the CDP system used in the perturbation test in this study, a previous study showed no significant difference in values after 3 or more trials [15], but we obtained the baseline value after 10 trials or more, including those in the preliminary test.

Custon et al. [16] reported that inhibition of balance function for unexpected perturbations after oral diazepam administration to elderly volunteers was due to inhibition of an automatic oligosynaptic spinal reflex via supraspinal modulation without conscious control. Therefore, our results may also be due to the same mechanism.

In addition to assessment of mean values, the percentage of all subjects showing recovery may be useful, because the pharmacodynamic and pharmacokinetic effects of benzodiazepine drugs widely vary among individuals. In this study, no subject recovered 40 min after intravenous midazolam injection, but recovery that would allow discharge by walking was observed in 50% of the subjects after 80 min and in most subjects after 100 min. The criteria to attain 90% recovery or more of the baseline value that were used in this study may be relatively strict. In the assessment of balance, these results may be interpreted as recovery that allows discharge without attendance. However, it is risky to guarantee complete recovery by one test type alone, and further evaluation is necessary.

In the assessment of the recovery of balance, the establishment of a reliable precise method is the most important. Next, a simple test that is highly correlated with the precise method in terms of results is necessary for wide clinical application [17]. A major advantage of the MSW test is that a correlation between balance and walking speed has been demonstrated [11,18,19]. In this study, a significant correlation was also observed between CDP and MSW test, but the correlation was only modest (0.67). This may be because the maximum walking ability reflects not only balance but also the entire motor function, including balance [20,21]. The second advantage is high reproducibility. In our preliminary study, the maximum discrepancy rate among four trials (difference between the maximum and minimum value/maximum value $\times 100$) was significantly lower ($P < 0.001$) in the MSW test ($6.72 \pm 3.58\%$) than in the USW test ($14.89 \pm 5.58\%$). We assume that stride length and cadence become constant in each person at the maximum speed, resulting in little variance in measurement values.

Appropriate assessment methods for recovery should be selected with consideration of the means of returning home. In door-to-door returning home, there is no need for complete recovery of walking ability as a discharge criterion, and the usual walking or standing tests may be adequate. However, when the end point is safe discharge with the patient walking, especially without attendance, even if patients can walk around slowly and steadily in the hospital, there is no guarantee that they will walk safely on the street, which is affected by various perturbation factors. The discharge criterion should reflect postural control ability for unexpected perturbation factors or, more safely, recovery of motor/balance function to more than usual walking ability. We believe that a dynamic balance test with unexpected perturbation stimuli is useful in assessing the balance-inhibitory effects of sedatives and that the MSW test can be a good simple dynamic balance test.

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