$P>0.2$). Furthermore, analysis of covariance (ANCOVA) was performed to compare R + L + B scores between diagnostic groups while controlling for gender, age, antidepressant prescription status, lithium dose, and antipsychotic dose. R + L + B scores were squared before the ANCOVA to obtain normal distribution (Shapiro–Wilk test: $P>0.1$). The antipsychotic dose was calculated as chlorpromazine equivalent in mg/day according to published guidelines (American Psychiatric Association, 1997; Inagaki et al., 1999). Statistical significance was set at two-tailed $P<0.05$. Analyses were performed using the SPSS version 11.0 (SPSS Japan, Tokyo).

3. Results

Table 1 shows the demographic and clinical characteristics, Purdue pegboard scores, and handgrip force test results. Age distribution did not differ across the three diagnostic groups. Although the average years of education were highest in the controls, there was no significant difference between unipolar and bipolar patients. Over 35% of unipolar patients and 60% of bipolar patients were prescribed lithium and/or antipsychotics. Antidepressants and anxiolytics were also prescribed in 69% and 59% of unipolar patients and 54% and 63% of bipolar patients, respectively. Patients with unipolar depression and bipolar disorder did not differ significantly in age at onset or in HDRS scores. The mean score of every subtest of the Purdue Pegboard was highest in the control group and lowest in the bipolar disorder group. Post hoc pairwise comparisons with Bonferroni corrections revealed that R + L + B scores were significantly higher in control subjects compared to unipolar and bipolar disorders and were significantly lower in bipolar disorder compared to unipolar depression. Patients with bipolar disorder also scored significantly lower in assembly subtest scores compared to control subjects, although the difference with unipolar depression did not reach statistical significance. No significant

Table 1
Clinical characteristics and Purdue pegboard and handgrip force test results.

	Healthy controls (N = 158)	Unipolar depression (N = 98)	Bipolar disorder (N = 48)	Statistical difference	Post hoc pairwise comparisons		
					Unipolar depression vs controls	Bipolar disorder vs controls	Unipolar depression vs bipolar disorder
Demographic characteristics							
Gender (male/female)	79/79	49/49	24/24	$\chi^2 = 0.00$, $P = 1.00$			
Average age (years)	44.6 (14.8)	44.4 (13.5)	44.5 (14.5)	$F = 0.004$, $P = 1.00$			
Education years	15.4 (2.4)	14.4 (2.5)	14.6 (2.8)	$F = 5.36$, $P = 0.0052$	**$t = 3.17$, $P = 0.0017$**	$t = 1.94$, $P = 0.054$	$t = 0.98$, $P = 0.67$
Age at onset	na	35.0 (13.1)	31.7 (13.3)	$t = 1.39$, $P = 0.17$			
HDRS-17	na	10.9 (7.0)	11.5 (7.0)	$t = 0.502$, $P = 0.62$			
Medication status							
Antipsychotics without lithium (%)	0.0	25.1	25.0				
Antipsychotics with lithium (%)	0.0	6.6	27.1				
Lithium without antipsychotics (%)	0.0	4.0	8.3				
Other psychotropics only (%)	0.0	41.0	18.8				
No psychotropic medication (%)	100.0	13.2	20.8				
Purdue pegboard							
Right hand	14.9 (2.1)	13.9 (2.0)	13.0 (2.2)	$\chi^2 = 30.3$, $P<0.0001$	**$U = 5751$, $P = 0.0005$**	**$U = 2022$, $P<0.0001$**	**$U = 1719$, $P = 0.0075$**
Left hand	14.1 (2.0)	13.3 (2.1)	11.9 (2.6)	$\chi^2 = 27.8$, $P<0.0001$	**$U = 6256$, $P = 0.0090$**	**$U = 1978$, $P<0.0001$**	**$U = 1614$, $P = 0.0019$**
Both hands	11.6 (1.9)	11.3 (2.1)	10.1 (2.2)	$\chi^2 = 27.9$, $P = 0.0001$	$U = 7160$, $P = 0.31$	**$U = 2273$, $P<0.0001$**	**$U = 1609$, $P = 0.0017$**
Right + left + both hands	40.6 (5.1)	38.4 (5.5)	35.0 (6.2)	$\chi^2 = 31.6$, $P<0.0001$	**$U = 6059$, $P = 0.0034$**	**$U = 1852$, $P<0.0001$**	**$U = 1594$, $P = 0.0016$**
Assembly	35.4 (8.0)	33.9 (8.6)	30.7 (9.3)	$\chi^2 = 12.4$, $P = 0.0020$	$U = 6576$, $P = 0.043$	**$U = 2617$, $P = 0.0011$**	$U = 1889$, $P = 0.053$
Handgrip force test							
Right hand	33.1 (9.2)	31.9 (10.7)	31.2 (8.4)	$\chi^2 = 1.95$, $P = 0.38$			
Left hand	31.3 (8.6)	29.6 (10.1)	29.5 (8.1)	$\chi^2 = 2.73$, $P = 0.26$			

na: not applicable.
Bold indicates Bonferroni corrected significance of $P<0.017$ in the post hoc analysis.

difference was observed between groups in the results of the handgrip force test. Comparison between bipolar I and bipolar II disorders did not result in significant difference in the pegboard scores. However, each bipolar subtype showed significantly lower scores in R+L+B compared to healthy controls and unipolar depression (bipolar I vs controls: $P=0.0046$, bipolar II vs controls: $P<0.0001$, bipolar I vs unipolar: $P=0.045$, bipolar II vs unipolar: $P=0.0054$; Mann–Whitney test).

Table 2 shows the results of the stepwise linear regression analyses with R+L+B or assembly scores as the dependent variable. Age and gender, as well as lithium and antipsychotic chlorpromazine equivalent dose, antidepressant and anxiolytic prescription status (i.e., 0=non-prescribed and 1=prescribed), and HDRS scores in patient groups, were included as predictor variables. Age was negatively correlated with R+L+B and assembly scores in all diagnostic groups. Lithium dose showed significant positive correlation with assembly scores in the unipolar depression group. On the other hand, antipsychotic dose was significantly negatively correlated with R+L+B and assembly scores in bipolar disorder group and with R+L+B score in unipolar depression group. Significant negative correlation between lithium dose and R+L+B in patients with bipolar disorder was also observed.

Table 3 shows the results of the ANCOVA comparing square-transformed R+L+B scores between diagnostic groups. Each pairwise comparison yielded a statistically significant result.

Table 2
The results of the stepwise regression analyses.

	Right+left+both			Assembly		
	β	t	P value	β	t	P value
Healthy controls						
Age	−0.14	−5.81	<0.0001	−0.24	−6.35	<0.0001
Gender	2.79	3.92	0.0001	2.71	2.38	0.018
Patients with unipolar depression						
Age	−0.10	−2.09	0.040	−0.25	−3.28	0.0015
Gender	na	na	na	na	na	na
Lithium dose	na	na	na	0.01	2.27	0.026
Antipsychotic (CP equivalent) dose	−0.01	−2.09	0.039	na	na	na
Antidepressant medication use	na	na	na	na	na	na
Anxiolytic medication use	na	na	na	na	na	na
HDRS score	na	na	na	na	na	na
Patients with bipolar disorder						
Age	−0.19	−3.68	0.0007	−0.36	−4.51	<0.0001
Gender	na	na	na	na	na	na
Lithium dose	−0.01	−2.27	0.028	na	na	na
Antipsychotic (CP equivalent) dose	−0.02	−3.01	0.0045	−0.02	−2.56	0.014
Antidepressant medication use	na	na	na	na	na	na
Anxiolytic medication use	na	na	na	na	na	na
HDRS score	na	na	na	na	na	na

CP: chlorpromazine; HDRS: Hamilton depression rating scale; na: not applicable (not included in the stepwise model).

Table 3
The ANCOVA pairwise comparisons of the transformed R+L+B scores of the Purdue pegboard between unipolar and bipolar patients and healthy controls.

	Unipolar depression vs controls		Bipolar disorder vs controls		Unipolar depression vs bipolar disorder	
	F value	P value	F value	P value	F value	P value
Intercept	257.8	**<0.0001**	185.7	**<0.0001**	111.2	**<0.0001**
Gender	21.0	**<0.0001**	15.0	**0.0001**	5.1	0.026
Age	33.2	**<0.0001**	42.0	**<0.0001**	9.1	**0.0030**
Lithium dose	0.0	0.87	1.8	0.18	1.0	0.32
Antipsychotic (CP equivalent) dose	4.6	0.032	8.2	**0.0046**	10.1	**0.0018**
Diagnosis	7.2	**0.0077**	15.4	**0.0001**	9.3	**0.0028**

ANCOVA was performed with the square-transformed R+L+B scores as the dependent variable, diagnosis as the independent variable, and gender, age, lithium dose, and chlorpromazine equivalent dose as covariates. Bold indicates Bonferroni corrected significance of $P<0.017$.
CP: chlorpromazine; ANCOVA: analysis of covariance.

4. Discussion

Comparison with healthy controls revealed that the gross movement dexterity assessed by the R+L+B score was impaired in both unipolar and bipolar disorder patients. Furthermore, the severity of impairment was significantly greater in patients with bipolar disorder compared to patients with unipolar depression. No significant difference in handgrip force across diagnostic groups suggested that poor performance in the pegboard test in patients groups was not due to reduced muscle strength. Antipsychotic medications had significant negative influence on the gross movement dexterity. However, the impairment of gross movement dexterity in unipolar and bipolar disorder patients remained significant even after controlling for the effects of antipsychotic and lithium medications. Fine fingertip dexterity assessed by the assembly subtest was significantly impaired in patients with bipolar disorder.

Previous studies reported fine motor dysfunction in bipolar patients even when they were euthymic (Langenecker et al., 2010; Wilder-Willis et al., 2001). Although the patients in the present study included those in depressive states, the depression severity assessed by HDRS was not significantly correlated with the outcome of the pegboard scores. Furthermore, patients with bipolar disorder showed more severely impaired dexterity compared to patients with unipolar depression, despite the similar severity of depressive symptoms. Therefore, our results also suggest that the motor dexterity in bipolar disorder patients is impaired regardless of the presence of depressive symptoms.

Some studies have also reported fine motor slowing in patients with unipolar depression (Pier et al., 2004a, b; Schrijvers et al., 2009), consistent with our results. However, studies comparing the fine motor function between unipolar and bipolar patients are scarce. Swann et al. (Swann et al., 1999) examined dexterity assessed by continuous tapping of the right index finger in patients with unipolar depression and bipolar disorder. Their results showed that depressed

patients with unipolar depression and bipolar disorder showed equally reduced tapping speed compared to healthy controls; however, bipolar disorder patients during manic state did not show significant difference compared to the controls. On the contrary, our results suggested that patients with bipolar disorder showed more severe impairment of motor dexterity compared to patients with unipolar depression irrespective of the severity of the depressive symptoms. The different results in the study by Swann et al. (Swann et al., 1999) may be due to the sample selection and the method of evaluating motor function. Participants of the study by Swann et al. were inpatients while our study included only outpatients with relatively low HDRS scores. Thus, more severe depressive symptoms may have influenced the dexterity test outcomes. Also, the use of Purdue pegboard allowed us to evaluate the gross movement dexterity of fingers, hands, and arms instead of the fine motor speed of a finger assessed by the finger tapping test.

The most interesting finding of the present study was that patients with bipolar disorder were more severely impaired in motor dexterity compared to unipolar patients with similar severity of depressive symptoms. Both bipolar I and bipolar II patients, despite the small number of patients with each subtype, showed significantly lower scores in R + L + B compared to unipolar depression. Although bipolar patients were more likely to be prescribed with antipsychotics and/or lithium, the difference between unipolar and bipolar depression remained statistically significant even when these medications were controlled for.

The functional difference strongly suggests different pathological conditions between the two disorders. Swann et al. (Swann et al., 1999) reported that the relationship between psychomotor impairment and catecholamine function may be stronger in bipolar depression than in unipolar depression. Thus, the severer impairment of dexterity observed in bipolar depression may be etiologically different from that of the unipolar depression. There are other possibilities that could explain the difference in impaired dexterity between unipolar and bipolar depression. First, some of the patients with unipolar depression in this study may go on to experience a manic/hypomanic episode and be rediagnosed as bipolar disorder. Such patients may have been the cause of decreased R + L + B scores in the unipolar depression group. Secondly, unipolar depression may lie on a continuum with bipolar disorder (Akiskal and Benazzi, 2006), and thus, may show slightly impaired dexterity compared to healthy controls. Future studies should assess the motor dexterity in bipolar spectrum conditions (Akiskal et al., 2000) to examine these possibilities.

Another finding from the study worth noting is that antipsychotic medication had significantly negative influence on motor dexterity, which was consistent with findings in a recent study of schizophrenic subjects (Sponheim et al., 2010). Physicians should keep in mind that antipsychotics, often prescribed for those with bipolar disorder as well as unipolar depression, may enhance the disability caused by the impairment of dexterity.

There are several limitations to this study. First, the cross-sectional design did not allow any definitive conclusions as to whether the impairment of the motor dexterity preceded or resulted from illness onset. Furthermore, some patients with unipolar depression in this study may be rediagnosed as bipolar disorder in the future, and thus follow-ups are necessary for accurate diagnosis. Secondly, the number of patients with bipolar disorder was small. Larger studies are needed to compare bipolar I and II disorders. Thirdly, as the patients were limited to those receiving outpatient treatments, our subjects might have been overrepresented by milder forms of illness. Moreover, we did not include bipolar patients during the manic episode. Further studies are necessary to determine whether dexterity is dependent on the phase of the disorder. Fourthly, the self-reported handedness was not verified using a validated hand preference questionnaire. A previous study has shown that non-right handedness is associated with soft bipolarity in mood disorders (Fasmer et al., 2008). Therefore, different rates of mixed-handed persons in each diagnostic group may have confounded the results of the pegboard test. However, since significant impairment of dexterity in bipolar disorder was observed in both the right hand and the left hand subtests, our conclusion that dexterity is impaired in bipolar disorder is not weakened by the possible inaccuracy of the handedness. Finally, the effects of medication could not be fully controlled due to the variability in types and doses. However, analyses examining the influence of antipsychotics and lithium on the outcome of the Purdue pegboard test indicated that these medications were not the only explanatory variable to the impaired dexterity.

In conclusion, we assessed manual motor dexterity in patients with unipolar depression and bipolar disorder and confirmed that both unipolar and bipolar patients were impaired in gross motor dexterity when compared to healthy controls. However, the severity of impairment was significantly greater in bipolar disorder compared to unipolar depression, despite the similar severity of depressive symptoms. The functional difference between unipolar and bipolar depression may suggest different pathological conditions between the two depressive disorders.

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Conflict of interest

The authors declare no conflicts of interest.

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