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Absence of differences in the learning rate of a speed–accuracy movement task between women patients with mild and major depression and healthy adult women

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ABSTRACT

This study tested the hypothesis that women patients with depression should perform movements more slowly and with greater variability, and their learning rate should be lower compared with age-matched healthy adult women. Three groups of adult women subjects (aged 33–37 years, women patients with mild and major depression and healthy adult women, n = 20 in each group) performed five series (20 repetitions in each series) of a speed–accuracy hand-movement task (SAT). The mean movement speed (V_a) of the SAT was lower and more stable (the coefficient of variation of V_a was lower) in women patients with major depression compared with those with minor depression and healthy adult women during the first series of the SAT. Only the V_a and movement accuracy (path of movement, S) of the SAT varied significantly in the five learning series regardless of the subject group (healthy women subjects and women patients with minor and major depression). The intraindividual variability of reaction time, V_a, maximal movement velocity to the target (tV_{max}), time to tV_{max}, and S did not change significantly in any of the groups. Our research data showed that although women patients with depression performed speed–accuracy movements more slowly, the stability of the performance of their movements and their learning rate did not differ from those of age-matched healthy adult women.

1. Introduction

Motivational and motor deficits are common in patients with depression and other psychiatric disorders and are related to symptoms of motor retardation (Felger & Treadway, 2017; Goldsmith et al., 2016; Pizzagalli, 2014). Major depressive disorder (MDD) is characterized by cognitive, decision-making, and memory and learning deficits (Cantone et al., 2017; Chen, Takahashi, Nakagawa, Inoue, & Kusumi, 2015; Dillon & Pizzagalli, 2018; Wagner, Müller, Helmreich, Huss, & Tadić, 2015). Considerable evidence suggests that MDD is associated with impaired brain signals of reward prediction error and expected value decreased reward sensitivity and learning (Chen et al., 2015; Victoria, Gunning, Bress, Jackson, & Alexopoulos, 2018). Meta-analyses indicate that volumetric reductions in the hippocampus, anterior cingulate cortex, prefrontal cortex, striatum, and amygdala are frequently observed in adults with depression (Gujral, Aizenstein, Reynolds, Butters, & Erickson, 2017). Three major functional modules, i.e., the default mode and the frontoparietal and sensorimotor networks, are commonly abnormal across MDDs (Sha et al., 2017).

To investigate motor learning, numerous studies have examined how individuals adapt their motor output according to trials

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(Shadmehr, Smith, & Krakauer, 2010; Wolpert & Flanagan, 2016; Wolpert, Diedrichsen, & Flanagan, 2011). Recently, it has been shown that such adaptation involves two memory processes: (1) a fast process, in which motor output both adapts and decays quickly, and (2) a slow process, in which it adapts and decays more gradually (Smith, Ghazizadeh, & Shadmehr, 2006; Ungerleider, Doyon, & Karni, 2002). While decreases or increases in these parameters have been documented in a variety of tasks (Shadmehr et al., 2010; Wolpert & Flanagan, 2016; Wolpert et al., 2011), it remains to be determined whether the time course of learning differs between healthy individuals and patients with mild and major depression.

It has been suggested that all intelligent agents balance response speed against accuracy in decision making (Heitz & Schall, 2012). This ability is a hallmark of decision making across species and tasks (Heitz & Schall, 2012; Salinas, Scerra, Hauser, Costello, & Stanford, 2014; Standage, Blohm, & Dorris, 2014; Thura & Cisek, 2016). One of the problems of learning is a trade-off between motor speed and accuracy (Elliott et al., 2010; Wolpert & Flanagan, 2016). In addition, an additional parameter is involved in this option, i.e., movement performance variability–stability, which is often determined by intraindividual performance variability (Shmuelof, Yang, Caffo, Mazzoni, & Krakauer, 2014; Solianik et al., 2018; Wolpert & Flanagan, 2016). It is generally accepted that when movement speed is preferred, accuracy decreases and the intraindividual variability of movements increases. Moreover, when accuracy and stability are preferred, speed is reduced (Wolpert & Flanagan, 2016). During motor learning, it is believed that the accuracy of the movement most often increases or the intraindividual variability decreases at the expense of a decrease in the speed of movement (Dayan & Cohen, 2011; Shmuelof et al., 2014).

Despite these previous studies, it currently remains unclear whether different movement performance strategies exist during learning and what strategies individuals with different health statuses choose during speed–accuracy decision-making tasks. Would they prefer speed at the expense of accuracy or accuracy at the expense of speed? In our study, the subjects were asked to perform a movement as fast and accurately as possible, and to react quickly. Therefore, our task can be said to have three aspects: i.e., reaction time, speed of movement, and accuracy of movement. Thus, the main aim of the study was to establish whether there were differences in learning strategies based on speed–accuracy movement task adaptation (learning) between healthy subjects and patients with mild and major depression. There is currently no doubt that physical exercise effectively reduces the symptoms of depression (Budde et al., 2018; Gujral et al., 2017; Kok & Reynolds, 2017).

Based on the studies cited above, we hypothesized that patients with depression should perform movements more slowly and with greater variability, and that their learning rate should be lower compared with the age-matched healthy adults.

2. Methods

2.1. Subjects

Twenty healthy adult women (age, 33.2 ± 5.7 years; body mass index [BMI], 27.9 ± 2.8 kg/m^2), 20 adult women patient with mild depression (Mild-DP, Beck Depression Scale score, < 16 points (average score, 6.2 ± 3.1); age, 35.6 ± 8.5 years; BMI, 28.9 ± 3.8 kg/m^2; disease duration, 9 ± 4 years), and 20 adult women patients with major depression (Major-DP, Beck Depression Scale score, > 16 points (average score, 21.2 ± 5.7 points); age, 34.6 ± 7.5 years; BMI, 27.9 ± 5.8 kg/m^2; disease duration, 8 ± 3 years) participated in the study. Women patients with minor-DP and major-DP were receiving antidepressant treatment as usual. All samples of patients were collected from Kedainiai outpatient mental care center, Kedainiai, Lithuania. The symptoms and signs of the women patients diagnosed with minor-DP or major-DP were evaluated by specialist physicians at the hospital. In addition, exclusion criteria included a history of smoking, drinking alcohol, hypertension, diabetes, acute infection, thyroid disorders, and nutrient supplementation. Healthy women participants were all healthy and untrained. Healthy participants were moderately physically active and participated regularly (at least 30 min three times per week) in recreational sports, but did not take part in any formal physical exercise or sports program in recent years. They were in self-reported good health, as confirmed by a medical history and physical examination. Each subject read and signed an informed consent form consistent with the principles outlined in the Declaration of Helsinki. The Ethics Committee of the Lithuanian University of Health Sciences approved this study.

2.2. Apparatus and measurement procedures

During the study, the participants were seated in a special chair at a table with a dynamic parameter analyzer (DPA–1) fastened to it (Skurvydas, Juodzbaliene, Darbutas, & Brazaitis, 2018; Solianik et al., 2018). The participant's back was straight and leaned against the backrest of the chair. Both arms were bent at an angle of 90° at the elbow joint so that the upper arms were against the sides of the DPA–1 support panel, with the forearms resting on it. The distance between the hands in the starting zone and the targets was 0.2 m. The position of the DPA–1 chair was adjusted so that the participant could sit comfortably in a standard position. The distance between the computer screen and the participant's eyes was approximately 0.7 m. The participant's right hand was attached to a joystick, through which the path and velocity of movements in the distal part of the hand were recorded. The sampling rate was 200 Hz. The handle at the end of the lever was adjusted to accommodate the participant's hand (the lever could move only in a horizontal plane). The target (a red circle with a diameter of 3.5 mm) appeared in the same place on the screen (the distance from the start zone to the target was 0.16 m) (Fig. 1).

2.3. Movement tasks

The participant had to perform various tasks using the right (dominant) hand: (a) a simple reaction task (SRT) (with a target with

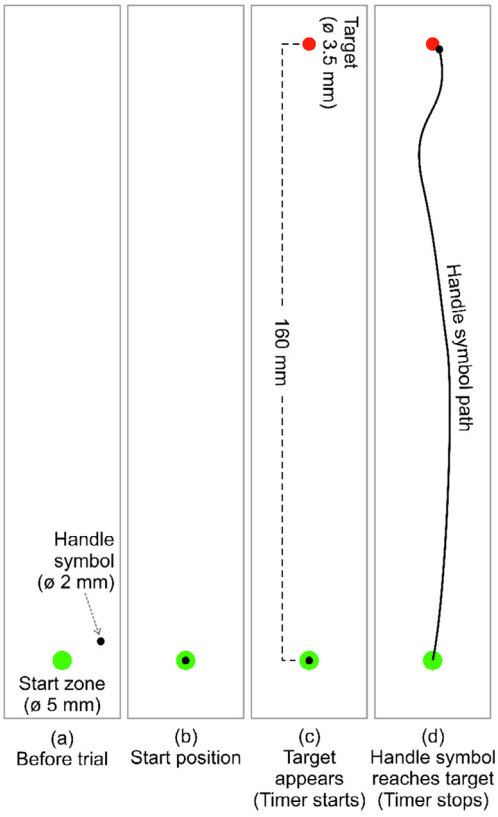

Fig. 1. Parameters of the speed–accuracy task (SAT).

a diameter of 3.5 mm appearing on the screen); (b) a maximal velocity performance task (MVT) (the subjects had to extend their hands as fast as possible and no accuracy was required); and (c) a speed–accuracy task (SAT) (the subjects had to react to the target that appeared on the computer screen as fast as they could and push the handle of the device, so that the circle of the handle symbol reached the target as fast as possible and followed the most accurate trajectory, and then stopped). The standard SAT instructions were: "Please give equal importance to speed and accuracy when completing this task. We would like you to respond as fast as possible while maintaining a high level of accuracy." Each task was repeated 20 times. The program generated a target on the computer screen intermittently (every 1–3 s). The sequential order selected was from the first to the third task. The time interval between the tasks was 2 min. The endpoint of the movement was recorded when the center of the handle symbol stopped in the circle and stayed there for no less than 0.02 s. During the SAT, the participant was required to position the handle symbol (diameter, 2 mm) in the start zone (the center of a 5 mm green circle) on the computer screen.

2.4. Motor learning procedures

After the SAT had been explained, the subjects performed three attempts, the results of which were not recorded. Subsequently, the task was performed in five series, each with 20 repetitions. The interval between the series was 1 min, but the repetitions in each series were performed without interruption. After each repetition, the subjects could see their result on the computer screen, and they were urged verbally to do their best.

2.5. Data and statistical analyses

The mean reaction time (RT), mean movement velocity (V_a), maximal movement velocity to the target (tV_{max}), time to tV_{max} (T_v) and handle transfer distance during the movement (S) (accuracy of movement) during 20 repetitions as well as the intraindividual variability (coefficient of variation, CV) of these variables in the SAT were calculated. Maximal movement velocity (V_{max}) and simple reaction time (sRT) were measured in the MVT and SRT, respectively.

The data were tested for normal distribution using the Kolmogorov–Smirnov test before conducting parametric statistics. The assumption about the homogeneity of variances was confirmed by the Levene's test and the assumption that the variance-covariance matrices are the same across the cells formed by the between-subject effects in Mixed ANOVA was confirmed by the Box's M test. The data are presented as mean and standard deviation (SD). A two-way mixed analysis ANOVA (General Linear Model) with baseline measures as a covariate was used to determine the effects of motor learning (from series-I-to-series-V) as within-subject factor of

Table 1
Hand-dominant movement variables in healthy adult women and adult women patients with mild (Mild-DP) and major (Major-DP) depression.

	Healthy	Mild-DP	Major-DP
sRT of SRT, s	0.225 ± 0.03	0.235 ± 0.01	0.235 ± 0.02
RT of SAT/sRT of SRT ratio, %	87.1 ± 9.1	87.2 ± 9.6	86.9 ± 7.3
V_{max} of MVT, $m{\cdot}s^{-1}$	1.49 ± 0.32	1.39 ± 0.35	1.24 ± 0.28
tV_{max} of SAT/V_{max} of MVT ratio, %	47.7 ± 8.6	44.6 ± 4.9	44.9 ± 9.3

RT of SAT, mean reaction time; sRT of SRT, simple reaction time; V_{max} of MVT, maximal movement velocity; tV_{max} of SAT, maximal movement velocity to the target. Values are means ± standard deviation (SD).

five levels and group condition (healthy women subjects vs women patients with mild-DP vs women patients with major-DP) as between-subject factor of three levels on the SAT variables. If significant main effects were found, Tukey's post-hoc test was performed to assess the sources of significant results across a set of conditions as between-subject factor and Bonferroni post-hoc tests were performed to assess the sources of significant results across a set of motor learning sessions as within-subject factor of five levels. Differences between groups for baseline state of motor performance (variables of SAT series-I; V_{max} of MVT; sRT of SRT; RT vs sRT; tV_{max} vs V_{max}) were analyzed via one-way analysis of variance using Tukey's adjustment for between-subject factor. For all ANOVAs, if Mauchly's test of sphericity was significant, then the Huynh-Feldt-correction was used as it is a more conservative measure of significance. Calculations of observed power (OP, as a percentage) were performed, and the partial eta squared (η_p^2) was estimated as a measure of motor learning and condition effect size. To avoid the inflation of the chance of making a Type 1 error in light of the number of tests conducted statistical significance was defined as $\eta_p^2 > 0.15$ and $P < 0.05$; Bonferroni-corrected p-values are reported (i.e., raw p-values multiplied with 15, to account for the 15 tests conducted across our ANOVAs, Cramer et al., 2016). Statistical analyses were performed using IBM SPSS Statistics for Windows (version 25.0, IBM Corp., Armonk, NY).

3. Results

3.1. Pre-learning state of motor performance

At baseline, there was no statistically significant difference between healthy adult women and adult women patients with mild-DP and major-DP regarding sRT of SRT and V_{max} of MVT (main group effect: $F_{2,57} = 1.92$ and 2.31, $\eta_p^2 = 0.031$ and 0.042, $P = 0.751$ and 0.871, $OP = 15$ and 19, respectively) (Table 1).

The baseline value for the speed of motor planning (RT) was significantly slower in the SAT compared with the sRT in the SRT (main motor task effect: $F_{2,57} = 36.14$, $\eta_p^2 = 0.265$, $P = 0.009$, $OP = 100$), with no significant group effect (main group effect: $F_{2,57} = 3.1$, $\eta_p^2 = 0.068$, $P = 0.617$, $OP = 21$) (Table 1 and Table 2). Similarly, the motor execution speed (tV_{max}) was significantly slower in the SAT compared with the V_{max} in the MVT (main test effect: $F_{2,57} = 29.23$, $\eta_p^2 = 0.191$, $P = 0.014$, $OP = 100$), with no significant group effect (main group effect: $F_{2,57} = 2.9$, $\eta_p^2 = 0.081$, $P = 0.653$, $OP = 26$). In addition, the difference between groups in the RT of SAT/sRT of SRT and tV_{max} of SAT/V_{max} of MVT ratios were not significant (main group effect: $F_{2,57} = 1.21$ and 1.89, $\eta_p^2 = 0.032$ and 0.039, $P = 0.889$ and 0.612, $OP = 14$ and 18, respectively) (Table 1).

In the series-I of SAT, there were no significant differences in the mean values between healthy adult women and adult women patients with mild-DP regarding CV of RT, V_a, tV_{max}, T_v, and S (post hoc for main group effect: $F_{2,57} = 1.72$, 1.34, 2.61, 0.98 and 1.24, $\eta_p^2 = 0.021$, 0.017, 0.038, 0.014 and 0.018, $P = 0.241$, 0.312, 0.141, 0.458 and 0.254, $OP = 15$, 10, 22, 14, and 12, respectively) (Table 2). However, V_a, the CV of V_a, and tV_{max} were lower and T_v was longer for patients with major-DP than compared with healthy adult women or with adult women patients with mild-DP (post hoc for main group effects: $F_{2,57} = 22.13$, 15.34, 19.87 and 18.7,

Table 2
Right-hand-dominant movement variables in the speed-accuracy task (SAT) of the first series of learning in healthy adult women and adult women patients with mild (Mild-DP) and major (Major-DP) depression.

	Healthy	Mild-DP	Major-DP
RT, s	0.257 ± 0.023	0.266 ± 0.037	0.269 ± 0.031
CV of RT, %	15.8 ± 5.8	13.7 ± 6.1	14.3 ± 4.3
V_a, $m{\cdot}s^{-1}$	0.234 ± 0.02	0.242 ± 0.044	0.212 ± 0.044[#]
CV of V_a, %	27.3 ± 4.8	31.8 ± 8.6	20.9 ± 6.9[#]
tV_{max}, $m{\cdot}s^{-1}$	0.630 ± 0.13	0.668 ± 0.18	0.542 ± 0.19[#]
CV of tV_{max}, %	12.3 ± 2.2	13.7 ± 3.2	14.5 ± 4.1
T_v, s	0.24 ± 0.04	0.224 ± 0.04	0.276 ± 0.045[#]
CV of T_v, %	20.1 ± 10.9	22.6 ± 13.5	22.7 ± 10.4
S, m	0.173 ± 0.013	0.170 ± 0.093	0.174 ± 0.093
CV of S, %	6.9 ± 2.9	6.1 ± 2.8	6.2 ± 3.2

[#] $P < 0.05$ compared with healthy adult women and adult women patients with mild-DP. RT, reaction time; V_a, mean movement velocity; tV_{max}, maximal movement velocity to the target; T_v, time to tV_{max}; S, handle transfer distance during the movement; CV (coefficient of variation), intraindividual variability in hand movement variables. Values are means ± standard deviation (SD).

η_p^2 = 0.214, 0.183, 0.197 and 0.174, P = 0.021, 0.034, 0.015 and 0.029, OP = 94, 85, 91 and 94, respectively).

3.2. Effects of mild and major depression on motor learning rate

A mixed two-way ANOVA revealed that over the course of the motor learning program all groups improved in V_a (main time effect: $F_{2,57}$ = 14.27, η_p^2 = 0.164, P = 0.032, OP = 86) and S (main time effect: $F_{2,57}$ = 8.78, η_p^2 = 0.152, P = 0.048, OP = 71), with no significant time × group interaction ($F_{2,57}$ = 2.3 and 2.9, η_p^2 = 0.032 and 0.046, P = 0.221 and 0.451, OP = 9 and 16, respectively). The absence of significance of time × group interaction for all variables measured throughout motor learning program indicates no between group differences in the motor learning rate ($F_{2,57}$ = 0.81–3.44, η_p^2 = 0.021–0.052, P = 0.152–0.569, OP = 5–21).

4. Discussion

We found that the movement speed (V_a) in the SAT was lower and more stable (the CV of V_a was lower) in women patients with major-DP compared with women patients with minor-DP and healthy adult women during the first series of a SAT. Second, we established that the average velocity and movement accuracy (path of movement, S) of the SAT changed significantly over five learning series (100 repetitions) in healthy women subjects and women patients with minor and major depression, regardless of subject group. To our knowledge, this is the first study that showed clearly that, although women patients with major depression carried out the SAT slower than did women patients with minor depression and healthy adult women, they exhibited no differences regarding sRT of SRT, V_{max} of MVT, RT of SAT, accuracy of movement (S of SAT), the intraindividual variability of these variables, and, most importantly, the learning rate.

Our research data coincide with the findings of other researchers, who showed that patients with depression perform movements more slowly (Felger & Treadway, 2017; Goldsmith et al., 2016); however, they do not coincide with studies that suggest that the intraindividual variability of movement performance is higher in patients with depression (Doumas, Smolders, Brunfaut, Bouckaert, & Krampe, 2012) and that the motor learning of patients with depression is worse than that of age-matched healthy individuals (Dillon & Pizzagalli, 2018; Pizzagalli, 2014). The slowing down in motor function (including a slowing down in motor learning) observed in patients with depression is believed to be associated with alterations in the corticostriatal neurocircuitry, which may reflect abnormalities in mesolimbic and mesostriatal dopamine, as well as an abnormal sensitivity to reinforcement during learning or decision-making and concomitant alterations in the dopaminergic corticostriatal circuitry (Dillon & Pizzagalli, 2018; Hamilton, Chen, Thomason, Schwartz, & Gotlib, 2011; Kaiser, Andrews-Hanna, Wager, & Pizzagalli, 2015; Pizzagalli, 2014). In addition, studies have shown that sensorimotor networks are commonly abnormal across MDDs (Adamaszek et al., 2017; Sha et al., 2017). For example, patients with MDD exhibited a lower gray matter density in the cerebellum (He et al., 2017), which is actively involved in the adaptation of movements under different conditions (Shadmehr et al., 2010; Wolpert & Flanagan, 2016).

It was recently established that patients with major depression show greater postural instability in dual-task performance on a stable platform. More importantly, they showed deficits in both working memory accuracy and postural stability with increasing posture task difficulty (moving platform) compared with healthy controls (Doumas et al., 2012). In our case, the intraindividual variability of movement variables in the SAT in women patients with depression was not greater than that observed for healthy women subjects. Moreover, the CV of V_a in women patients with major depression was significantly lower than that recorded in women patients with mild depression and healthy women subjects. We can only speculate that women patients with major-DP chose a less-risky movement strategy during speed-accuracy task, i.e., they performed movements at a lower speed to ensure the movement accuracy and the stability of the performance (Table 2); thus, this may suggest that chosen movement strategy may ensure safer movement performance (i.e. reduced probability for injury) for women patients with major-DP. However, this contradicts the findings of other researchers, which suggest that patients with major-DP exhibit higher motor and attentional impulsivity (Ponsoni et al., 2018) and worse executive functions, i.e., worse inhibition of unnecessary stimuli (Snyder, 2013; Sonuga-Barke, Cortese, Fairchild, & Stringaris, 2016).

We believe that the greatest novelty of our research is that we found an absence of differences in learning—sensorimotor adaptation—strategies between women patients with mild and major DP and healthy adult women. As suggested recently, being explicit, the learning process is likely to rely on a wide network of attentional, executive, and motor areas (Huberdeau, Krakauer, & Haith, 2015). We established that the healthy adult women and women patients chose a learning strategy of speed and accuracy: i.e., they performed movements faster (by 10–18%) and more accurately (by 3–4%). During the adaptation-based learning of SAT, healthy adult women and the women patients exhibited improvements in both speed and accuracy of movement, although the intraindividual variability did not change significantly. Even performance of 100 repetitions of fast and accurate movement can evoke sufficient changes in brain plasticity (Micheli, Ceccarelli, D'Andrea, & Tirone, 2018; Gourgouvelis, Yielder, & Murphy, 2017), and SAT could be an effective tool for motor performance prevention not only for healthy women, but also for reducing the symptoms of depression in women with minor or major depression.

In our research, the CVs of movement variable learning were unexpectedly not decreased (Fig. 2B, D, F, H, and J). When movements must be performed in a fast and accurate manner, an additional motor control determinant becomes an important “player”: i.e., the variability of motor performance. According to Harris and Wolpert (1998), the minimum variance theory accurately predicts the trajectories of movements and the speed–accuracy trade-off described by Fitts law. Moreover, Bertucco, Bhanpuri, and Sanger (2015) showed that intrinsic motor variability modulates the SAT trade-off. Our research participants had to learn decision-making during the SAT because the ability to trade speed and accuracy off against each other is a hallmark of decision-making across

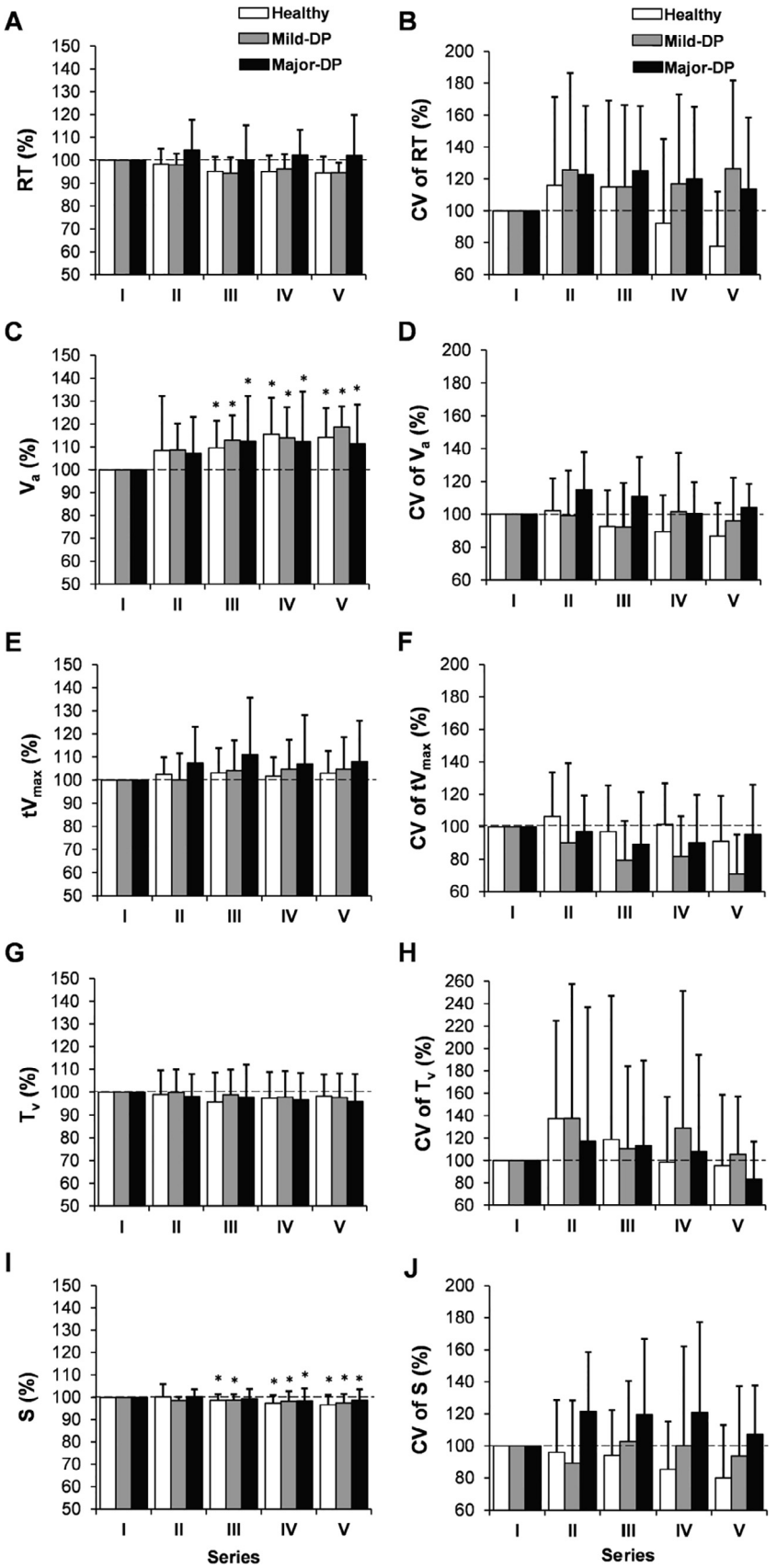

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Fig. 2. Time-course of mean reaction time (RT) (A) and the intraindividual variability (CV) of RT (B), mean movement velocity (V_a) (C) and the CV of V_a (D), maximal movement velocity to the target (tV_{max}) (E) and the CV of tV_{max} (F), time to tV_{max} (T_v) (G) and the CV of T_v (H), and the handle transfer distance during the movement (S) (I) and the CV of S (J) over five series of a speed–accuracy task in healthy adult women and adult women patients with mild depression (Mild-DP) and major depression (Major-DP). * $P < 0.05$ compared with Series-I. Values are means ± standard deviation (SD).

species and tasks (Salinas et al., 2014; Thura & Cisek, 2016). This decision-making process undoubtedly involved both cognitive and motor aspects (Thura & Cisek, 2016). Intraindividual variability is commonly the fundamental measure of change in human motor behavior (Kyguoliene et al., 2017; Solianik et al., 2018) and cognitive performance capacity (Graveson, Bauermeister, McKeown, & Bunce, 2016; Hultsch, MacDonald, & Dixon, 2002; Yao, Stawski, Hultsch, & MacDonald, 2016). Until recently, motor variability was viewed as an unwanted feature of movements, i.e., noise that the brain is able to reduce only with practice (Shmuelof et al., 2014). However, Wu, Miyamoto, Gonzalez Castro, Ölveczky, and Smith (2014) showed that task-relevant motor variability, which was measured at the baseline before the subjects were exposed to a novel motor task, can be used to predict the rate of learning in the task. What should be the optimal variability of movement performance during the learning SAT and how it depends on the degree of depression remains to be clarified.

One limitation of the present study is that in our study we included only young adult women patients diagnosed with mild or major depression, which were compared with young healthy women. The anatomical and hormonal differences between men and women (Stephenson & Kolka, 1993; Janssen, Heymsfield, Wang, & Ross, 2000; Van Marken Lichtenbelt et al., 2009), and children (Gorianovas et al., 2013), and weakened neuromuscular system response to exercise conditions in older people (Brazaitis et al., 2019), and considering that women are more susceptible to depression than men (Ma, Xu, Wang, & Li, 2019), suggest that the results of the present study may not be directly applicable to adult men, children, or older people.

In conclusion, our research data showed that although women patients with depression performed speed–accuracy movements more slowly, the stability of the performance of their movements, as well as their learning rate, did not differ from those of aged-matched healthy adult women. Therefore, we believe that learning of movements can be applied not only as a preventive measure, but also as a curative measure for women patients with varying degrees of depression. Moreover, it has been found that physical exercise stimulates the expression of the brain-derived neurotrophic factor, which stimulates brain plasticity and cognitive function in healthy subjects (Skurvydas et al., 2017; Verbickas et al., 2017) and in patients with depression (Budde et al., 2018; Duman & Monteggia, 2006).

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the local Ethics Committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent

Written informed consent was obtained from all participants included in the study.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humov.2019.05.016.

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