Co-variation of Depressive Mood and Spontaneous Physical Activity Evaluated by Ecological Momentary Assessment in Major Depressive Disorder

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Abstract— The objective evaluation of depressive mood is thought to be useful for the diagnosis and treatment of depressive disorders. Thus, we investigated psychobehavioral correlates, particularly the statistical associations between momentary depressive mood and behavioral dynamics measured objectively, in patients with major depressive disorder (MDD). Patients with MDD (n = 14) wore a watch-type computer device and rated their momentary symptoms using ecological momentary assessment. Spontaneous physical activity in daily life, referred to as locomotor activity, was also continuously measured by an activity monitor built into the device. A multilevel modeling approach was used to model the associations between changes in depressive mood scores and the local statistics of locomotor activity simultaneously measured. The statistical model constructed indicated that worsening of depressive mood was associated with increased intermittency of locomotor activity, as characterized by a lower mean and higher skewness. Our findings suggest the presence of associations between momentary depressive mood and behavioral dynamics in patients with depression, which may lead to the continuous monitoring of the pathological states of MDD.

I. INTRODUCTION

Major depressive disorder (MDD) is a psychiatric disorder that is characterized by the presence of mood disturbances (either depressed mood or a loss of interest or pleasure in daily activities) consistently for more than several weeks [1]. In addition to these mood disturbances, behavioral alterations, including diminished activity, loss of energy, and psychomotor retardation or agitation, are remarkable co-occurring symptoms [1]. Although many prior studies focused only on these behavioral alterations of physical activity levels [2, 3] or their rhythmicity [2, 4, 5], the complete details of dynamical properties, which may contain richer information regarding pathological states, have not been examined.

We recently measured the so-called locomotor activity, i.e., the spontaneous physical activity in daily life, for >1 week in patients with MDD and reported that depressive patients exhibited more intermittent behavioral patterns that were characterized by reduced mean activity levels associated with occasional bursts of locomotor activity compared with healthy subjects [6, 7]. These findings suggest that the statistical properties of intermittent locomotor dynamics are important and useful objective markers of MDD, and there is a novel possibility of continuously monitoring the pathological states of this disorder based on behavioral dynamics. However, although these studies were successful in providing a biobehavioral measure for MDD based on long-term locomotor activity data, this is not sufficient for continuous monitoring because of the lack of temporal resolution and correlation with symptoms (e.g., subjective depressive mood). To capture rapid changes in pathological states in much shorter time frames (e.g., daily or within-day scales), which may provide important information on clinical conditions or the efficacy of clinical treatments, other types of approaches are required.

Therefore, in this study, we investigated the temporal associations between depressive mood and behavioral dynamics in MDD patients using ecological momentary assessment (EMA) [8]. Specifically, we examined covariate properties between within-individual temporal changes in depressive mood scores and local statistics of locomotor activity around the recordings of self-reported symptoms. Showing such associations is considered to be important because it allows us to estimate the changes in depressive mood continuously from locomotor activity, which can be measured in a truly continuous manner, providing valuable insights into the pathological states of MDD.

II. METHODS

A. Subjects

The data were acquired from 14 patients with MDD [12 males (M), two females (F); age, 34.0 ± 5.7 years; age range, 22–42 years]. The patients with MDD were outpatients of the Teikyo University Mizonokuchi Hospital, Kanagawa, Japan, and their locomotor activity data have been published elsewhere [6, 7]. The patients who applied for participation in the study were interviewed and screened by a well-trained psychiatrist. The inclusion criteria were as follows: a

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diagnosis of MDD according to the Diagnostic and the Statistical Manual of Mental Disorders (DSM)-IV [1]; information on the current depressive episode; and age between 20 and 55 years. The exclusion criteria were: current substance abuse and other psychiatric diseases; lifetime history of schizophrenia or personality disorder; or severe physical illness. The 17-item Hamilton Depression Rating Scale (HDRS) [9] was also administered to all the patients [13.3 (mean) ± 2.9 (SD); range, 8.8–18.5]. The detailed profiles of the patients are summarized in Table I. All patients were given a full explanation of the purposes and potential risks of the study by well-trained researchers and their primary psychiatrists confirmed that they had a capacity to consent. Subsequently, they signed an institutionally approved informed consent form. This study was approved by the research ethics committees of Teikyo University and the University of Tokyo.

B. Assessment of Depressive Mood and Locomotor Activity

We used an EMA technique [8] to record momentary symptoms in the patients, which allows us to address subjects' behaviors, psychological states, and physiological reactions at multiple time points as the individual experiences in daily life. The collection of data in natural settings can enhance the validity of measurements, thus avoiding the pitfalls of retrospective recall, which highly distort self-reported data collection.

A small watch-type computer (Ruputer, ECOLOG, 42 g; Seiko Instruments Inc., Tokyo, Japan) was used as an electronic diary to record self-reported symptoms [10]. Patients with MDD were requested to record their momentary symptoms by answering EMA questionnaires over the study period (37.43 ± 14.82 days; range, 18–67 days). EMA questionnaires prompted the patients to record their symptoms via a beep signal at randomly selected times within ±36 min of

TABLE I. PROFILES OF PATIENTS WITH MAJOR DEPRESSIVE DISORDER

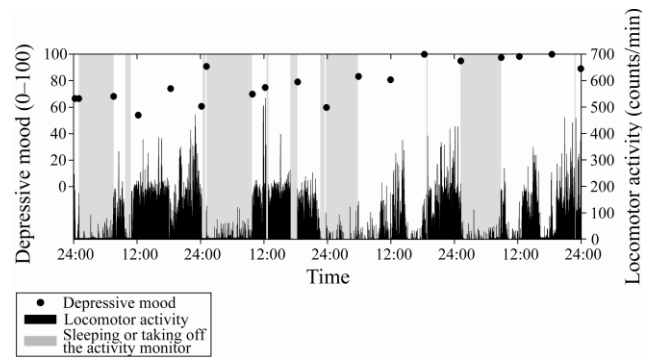| Patient No.	Gender [male(M)/ female (F)]	Age	Employed [yes (Y)/ no (N)]	Disease duration (month)	HDRS score (17 items)
1	M	42	Y	135	12
2	M	35	N	7	11.2
3	F	33	N	36	18.5
4	M	37	N	34	10
5	M	33	N	10	12.8
6	M	35	N	19	8.8
7	M	32	N	18	15.5
8	M	26	Y	69	13
9	F	22	N	22	12.4
10	M	33	Y	33	18.1
11	M	29	Y	7	10.8
12	M	38	N	21	13
13	M	40	N	2	16.8
14	M	41	Y	36	13

HDRS: Hamilton Depression Rating Scale

Fig. 1. Fluctuations of depressive mood scores and locomotor activity. Filled circles indicate depressive mood scores recorded by ecological momentary assessment over four consecutive days in a patient with major depressive disorder. Their simultaneously measured locomotor activities are also shown. The periods during which they were sleeping or had taken off the device are shaded in gray.

the predefined times (6:00, 12:00, 18:00, and 24:00) during waking periods. In addition to these scheduled times, all patients were also requested to register the time at which they woke up or went to bed as well as their momentary symptoms (Fig. 1).

The EMA questionnaires assessed subjective mood states and the intensity of physical symptoms (fatigue, sleepiness, pain, etc.) using a visual analog scale (0–100 with 5-point intervals). The mood states were rated using the Depression and Anxiety Mood Scale (DAMS) [11], which was developed to measure anxious and depressive moods as separately as possible. In this study, we focused on the depressive mood because depressive symptoms are the most prominent feature of MDD, and mood changes are consider an important pathological states of the disease.

The watch-type device used for this study also equipped with an acceleration sensor which is compatible with that of the commercial actigraph (Ambulatory Monitors Inc., Ardsley, NY, USA). All patients wore this device on the wrist of their respective non-dominant hand throughout the study period. The sensor for assessing locomotor activity is a uni-axial piezo-electronic accelerometer that is capable of detecting even small changes in bodily movements (≥0.01 G/rad/s) in daily life. Zero-crossing counts accumulated for every 1 min were used as locomotor activity data (Fig. 1). Locomotor activity data collected during periods in which the patients were not wearing the device or sleeping were excluded from the analysis.

C. Data Analysis: Local Statistics of Locomotor Activity

We focused on the first- and third-order statistical moments (i.e., mean and skewness) of locomotor activity data because the combination of these statistics can well characterize the intermittent or bursty nature (i.e., reduced activity levels and occasional bursts leading to a positively skewed probability distribution) of the data. Indeed, in our previous study [12], we considered a variety of local statistical indices as a feature to characterize the increased intermittency of local locomotor activity, and found that the combination of lower mean levels and higher positive skewness were shown to be most effective. Therefore, we modeled the concurrent associations between depressive mood and the local statistical

	Coefficient (*SE*)	*F* value	*p* value
Intercept (γ_{00})	64.09 (5.53)		<0.001
Coefficient of the local mean (γ_{10})	−0.05 (0.03)	$F_{1,750} = 3.23$	0.073
Coefficient of the local skewness (γ_{20})	2.32 (0.93)	$F_{1,750} = 6.18$	0.013
Coefficient of the local mean × local skewness (γ_{30})	−0.02 (0.01)	$F_{1,750} = 4.07$	0.044

SE: standard error. The statistical model is as follows: Depressive mood scores$_{ij}$ = γ_{00} + γ_{10} (Mean$_{ij}$) + γ_{20} (Skewness$_{ij}$) + γ_{30} (Mean$_{ij}$ × Skewness$_{ij}$) + ζ_{0i} + ζ_{1i} (Mean$_{ij}$) + ε_{ij}

properties of locomotor activity by using the mean and skewness as the statistics which were calculated from locomotor activity data with a length of 60 min centered around each EMA recording: the time window which was found to be most effective in studying the associations [12].

D. Statistical Analysis: Statistical Model for Depressive Mood

We adopted a multilevel modeling approach, which is an extension of traditional regression models and has been recommended for analyzing data with a hierarchical structure, including EMA data [13]. All multilevel models were estimated using SAS Proc Mixed (SAS 9.2, SAS Institute Inc., Cary, NC). A *p* <0.05 was considered significant.

We identified the statistical model that described the associations between depressive mood scores and the local statistics of locomotor activity. We compared all possible multilevel models that consisted of a linear combination of a subset of both local statistics and their interaction. In addition, we examined both fixed and random effects for each predictor in each model. The specification of considered models is as follows:

Level 1 equation (within-individual level):
$$Y_{ij} = \pi_{0i} + \sum_{k=1}^{n} \pi_{ki} X_{ij} + \varepsilon_{ij} \quad (1)$$
Level 2 equations (between-individual level):
$$\pi_{0i} = \gamma_{00} + \zeta_{0i} \quad (2)$$
$$\pi_{ki} = \gamma_{k0} + \zeta_{ki} \ (k = 1, ..., n) \quad (3)$$
Combined model:
$$Y_{ij} = \gamma_{00} + \sum_{k=1}^{n} \gamma_{k0} X_{ij} + \zeta_{0i} + \sum_{k=1}^{n} \zeta_{ki} X_{ij} + \varepsilon_{ij} \quad (4)$$

where Y_{ij} indicates the dependent variable (depressive mood) at the *j*th EMA recording for the *i*th subject; X_{ij} is the predictor (local statistics of locomotor activity) corresponding to the *j*th EMA recording for the *i*th subject; π_{0i} and π_{ki} are the subject *i*'s intercept and coefficient (i.e., slope) of the predictor, respectively; γ_{00} is the average intercept across all subjects; γ_{k0} is the average slope across all subjects; the random terms ζ_{0i} and ζ_{ki} are the between-individual residuals; and ε_{ij} is the within-individual residual. All variance components were assumed to follow a normal distribution with zero mean. We used the deviance test to compare the goodness-of-fit of the models.

After identifying the group statistical model, we further constructed the personalized models by optimizing it to individual data. In this optimization process, the model parameters were personalized to minimize wide individual differences, such as lifestyle, pathological conditions, and effects of antidepressant medication. The model parameters were optimized individually using data collected at one week in the early part of the measurement. Subsequently, the depressive scores in another week in the later part of the study were estimated by substituting the local statistics of locomotor activity into the personalized model. All random terms in the model were set to zero because of their definition. The estimation was evaluated by examining the correlation coefficient between estimated and self-reported depressive mood scores.

III. RESULTS

A. Recording Profiles

We obtained 1921 [137.2 (mean) ± 63.6 (SD) per person] EMA recordings from patients with MDD. If simultaneous locomotor activity data were not acquired properly because of trouble with or removal of the device, we excluded the data from the analysis. Finally, we obtained 767 (54.8 ± 23.3) sets of simultaneous recordings of EMA and locomotor activity data. The mean level and its standard error (*SE*) of depressive mood was 58.95 ± 2.73 and those of the mean activity level were 111.59 ± 5.08. The values of skewness were 0.47 ± 0.07.

B. Determination of the Statistical Model for Depressive Mood

The statistical model identified was a linear combination of the local mean, skewness, and their interaction as predictors, in which the local mean and intercept had a random effect: Depressive mood scores$_{ij}$ = γ_{00} + γ_{10} (Mean$_{ij}$) + γ_{20} (Skewness$_{ij}$) + γ_{30} (Mean$_{ij}$ × Skewness$_{ij}$) + ζ_{0i} + ζ_{1i} (Mean$_{ij}$) + ε_{ij}. All the coefficients in patients with MDD were significant, with the exception of the coefficient of the local mean of locomotor activity (Table II) with a significant positive value ($\gamma_{20} = 2.32 \pm 0.93$, $p = 0.013$) for skewness and negative values for both the mean ($\gamma_{10} = -0.05 \pm 0.03$, $p = 0.073$) and their interaction ($\gamma_{30} = -0.02 \pm 0.01$, $p = 0.044$). These results indicate the presence of a significant association between increased intermittency of locomotor activity and worsening of self-reported depressive mood. The negative coefficient of interaction term possibly reflects situations in which the depressive mood becomes worse with both lower activity levels and positively larger skewness; thus, more frequent episodes of bursts are observed.

C. Estimation of Depressive Mood by Personalized Models

We estimated the depressive mood scores by statistical model identified with the personalized model parameters. Fig. 2 shows examples of the estimation of depressive mood from local statics of locomotor activity. The personalized parameter values for the patient A were: $\gamma_{00} = 83.78$, $\gamma_{10} =$
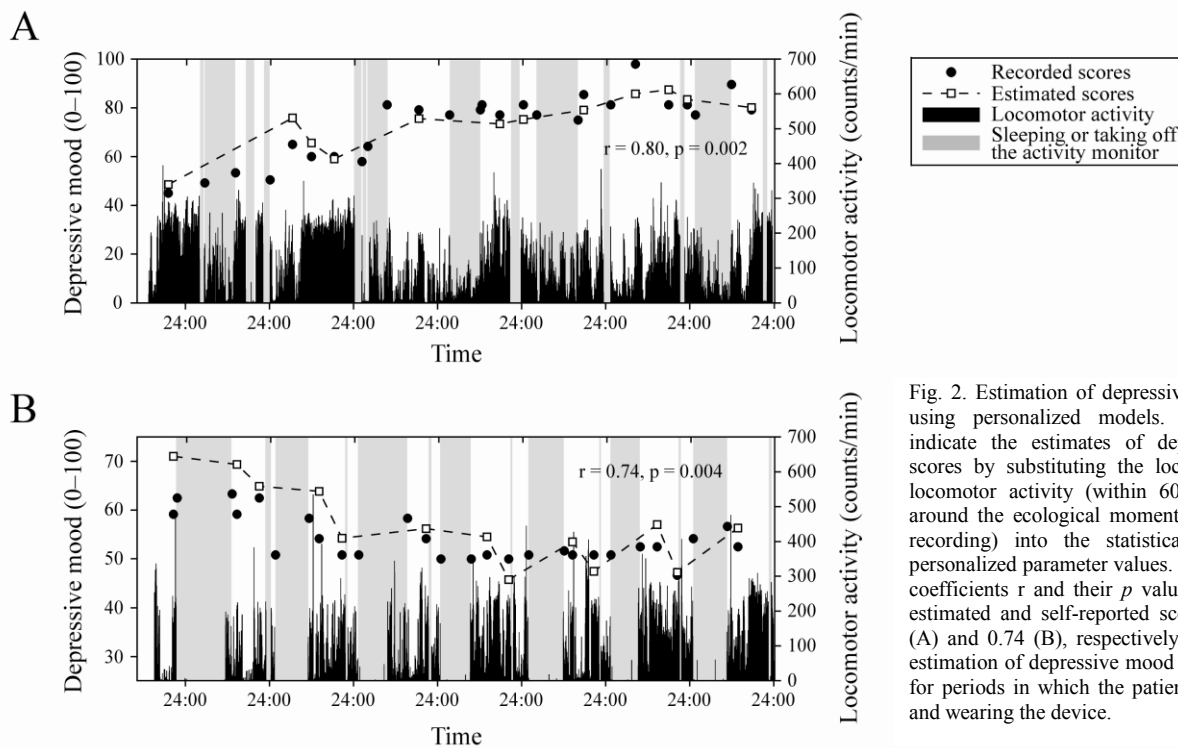
Fig. 2. Estimation of depressive mood scores using personalized models. Open squares indicate the estimates of depressive mood scores by substituting the local statistics of locomotor activity (within 60 min centered around the ecological momentary assessment recording) into the statistical model with personalized parameter values. The correlation coefficients r and their *p* values between the estimated and self-reported scores were 0.80 (A) and 0.74 (B), respectively. Note that the estimation of depressive mood was only made for periods in which the patients were awake and wearing the device.

-0.08, $\gamma_{20} = 1.17$, and $\gamma_{30} = -0.01$ (Fig. 2A), whereas those for the patient B were: $\gamma_{00} = 70.38$, $\gamma_{10} = -0.15$, $\gamma_{20} = 4.08$, and $\gamma_{30} = -0.06$ (Fig. 2B). In these two patients, the correlation coefficients between self-reported and estimated depressive mood scores were considerably high [r = 0.80 ($p = 0.002$) for the patient A and r = 0.74 ($p = 0.004$) for the patient B]. Although we were unable to perform this optimization procedure for the data from all patients because this requires relatively long-term measurements (>2 weeks), we confirmed the correlation coefficients ranging from 0.48 to 0.80 in six patients. The personalization of the model structure and other sophisticated optimization methods would probably highly improve the estimation.

IV. CONCLUSION

We demonstrated the presence of associations between momentary depressive mood and behavior dynamics in patients with MDD. These results suggest that it is possible to objectively estimate a momentary depressive mood based on changes in physical activity, thus leading to continuous monitoring of the pathological states of MDD.

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