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Multiple time measurements of multidimensional psychiatric states from immediately before the COVID-19 pandemic to one year later: a longitudinal online survey of the Japanese population

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The coronavirus disease 2019 (COVID-19) pandemic has profoundly affected the mental health of both infected and uninfected people. Although most psychiatric disorders have highly overlapping genetic and pathogenic backgrounds, most studies investigating the impact of the pandemic have examined only single psychiatric disorders. It is necessary to examine longitudinal trajectories of factors that modulate psychiatric states across multiple dimensions. About 2274 Japanese citizens participated in online surveys presented in December 2019 (before the pandemic), August 2020, Dec 2020, and April 2021. These surveys included nine questionnaires on psychiatric symptoms, such as depression and anxiety. Multidimensional psychiatric time-series data were then decomposed into four principal components. We used generalized linear models to identify modulating factors for the effects of the pandemic on these components. The four principal components can be interpreted as a general psychiatric burden, social withdrawal, alcohol-related problems, and depression/anxiety. Principal components associated with general psychiatric burden and depression/anxiety peaked during the initial phase of the pandemic. They were further exacerbated by the economic burden the pandemic imposed. In contrast, principal components associated with social withdrawal showed a delayed peak, with human relationships as an important risk modulating factor. In addition, being female was a risk factor shared across all components. Our results show that COVID-19 has imposed a large and varied burden on the Japanese population since the commencement of the pandemic. Although components related to the general psychiatric burden remained elevated, peak intensities differed between components related to depression/anxiety and those related to social withdrawal. These results underline the importance of using flexible monitoring and mitigation strategies for mental problems, according to the phase of the pandemic.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has affected all aspects of society globally [1, 2]. Given its profound impact on the mental health of both infected and uninfected persons, there is a greater need for mental health science [3–6]. Indeed, various psychiatric states, such as depression [7], general anxiety [8], panic disorder [8], social anxiety disorder [9], alcohol [10], internet-related problems [11], adult attention-deficit/hyperactivity disorder (ADHD) [12], and autism spectrum disorder (ASD) [13] have been exacerbated during COVID-19. Several studies including a meta-analysis reported exacerbations of mental health due to the pandemic [14, 15] while concluding that there was no clear association with psychiatric disorders [16, 17]. This may indicate that the impact of the pandemic is heterogeneous, both geographically (Some countries experienced stronger waves than others.) and temporally (Cases rise and fall in waves, so the effects

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of stress on people vary with the passage of time since the stress exposure.) To prevent further deterioration and persistence after the pandemic subsides, a comprehensive understanding of longitudinal trajectories of multidimensional psychiatric states during this pandemic is required.

To achieve a full grasp of the pandemic effects on mental health, it is necessary to evaluate data that include pre-pandemic data as a baseline, and multiple psychiatric states. First, baseline control data are essential to directly assess any pandemic effects. Most evidence to date is based on cross-sectional samples and very few studies have included data from immediately before the pandemic [10, 18–21]. Second, multiple time points during the COVID-19 pandemic should be included. This is because some psychiatric symptoms, such as depression and anxiety, react to the initial stages of events such as natural disasters, including the pandemic [7, 22–24], while others, such as suicide, show delayed reactions [25–27]. Indeed, both patterns have been observed during this pandemic. The increase in suicides due to the pandemic is not yet clear worldwide but has been confirmed in several countries, and delayed onsets are of concern internationally [28, 29]. Third, multiple psychiatric states should be addressed simultaneously in the same population, since psychiatric disorders have highly overlapping genetic backgrounds and pathogenesis [30, 31], and a shift from categorical to the dimensional classification of psychiatric disorders has long been advocated [32, 33]. Generally speaking, psychiatric disorders can be decomposed into three robust factors that interact strongly; (1) anxiety and depression (internalizing), (2) substance dependence, antisocial personality disorder, and conduct disorder (externalizing), (3) bipolar disorder and schizophrenia (psychotic experience) [34–36]. Furthermore, some have even proposed that these three latent traits represent different manifestations of a single, general, psychopathological dimension called the "p factor" [30, 37, 38]. Thus, multiple studies have suggested the existence of a robust, parsimonious structure in psychiatric disorders. Is it possible then to decompose psychiatric disorders into several (or even single) factors or components, depending on how they have

been affected by the COVID-19 pandemic? If so, how do such components relate to pre-pandemic components?

By analyzing data before and during the pandemic, and by gathering data about nine psychiatric states, we identified four underlying principal components (PCs). Of these, three PCs showed distinct exacerbation trajectories, with different risks and protective factors. The results of this study may help to optimize strategies to improve mental well-being in at-risk populations.

SUBJECTS AND METHODS
Procedures and outcomes
We conducted a repeated online survey with the help of Macromill Inc. (Japan) (See Supplementary Methods for details). The original survey was conducted in December 2019. Since the first COVID-19 case was not identified in Japan until January 2020, data from this survey are considered baseline data (T0). In response to the COVID-19 pandemic, individuals from this survey were invited to participate in follow-up surveys that took place in August 2020 (T1), December 2020 (T2), and April 2021 (T3). In these follow-up surveys, several items were added regarding COVID-19 [11, 39]. Multidimensional psychiatric data taken immediately before and during the COVID-19 pandemic were collected from a total of 4680 participants. We excluded 326 individuals because of inconsistencies or contradictions in their answers (details in Supplementary Methods). An additional 419 individuals were excluded because they responded identically to all items, using only the maximum or minimum values in the questionnaires, including reversed questions. Among the remaining 3935 individuals, 1661 participated in only two or three surveys. In the end, 2274 individuals who responded to all four surveys comprised the main study population. We defined the main study population in this fashion so as to avoid any influence driven by post hoc estimation of missing entries due to nonresponders. Applying a principal component analysis (PCA) to data including such estimated values might change the estimated principal components. Therefore, generalized linear model (GLM) regression analyses on the identified PCs were also primarily performed with this main study population, which excluded partial data. We further repeated these GLM analyses with a survey population that included partial data to rule out influences due to dropout from the surveys ($N = 3935$; survey population). (Fig. 1). Selection of the time point was determined by
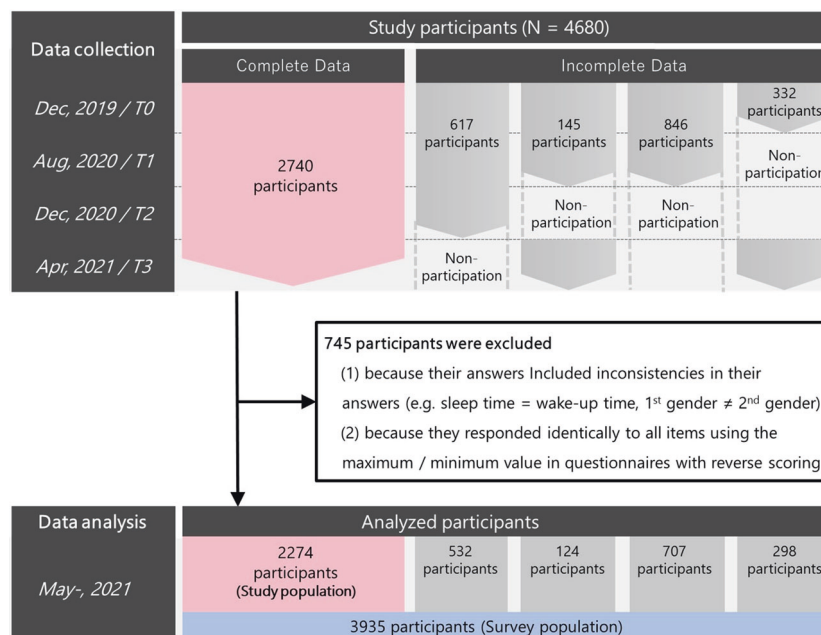

Fig. 1 Selection into cohorts. 4680 participants participated in the T0 survey immediately before and during the COVID-19 pandemic. 745 participants were excluded due to data problems and 3935 participants remained in the analysis and were defined as the "survey population." Of the 3935, 1661 participated in only two or three surveys (incomplete data) (532, T0-T2; 124, T0-T1, T3; 707, T0-T1; 298, T0 and T3). Therefore, 2274 respondents completed all four surveys and were defined as the "study population".

considering the following criteria: (1) the timing of acquisition should overlap with the peak of infection as much as possible (2) the interval between each acquisition of follow-up data should be as similar as possible. The actual time points were determined by monitoring the infection situation in real-time, in order to satisfy the above requirements, while keeping in mind that predicting the infection situation in advance is difficult. A detailed explanation is provided in Supplementary Methods. The original and follow-up research designs were approved by the Ethics Committees of the Advanced Telecommunications Research Institute International (ATR) (approval No. 21-195 for the original study and 21-749 for the follow-up study). All participants read a full explanation of the study and gave informed consent before each survey.

Demographic variables were collected as follows: sex (women and men), age, job status (self-employed, employed, unemployed, and other), education history, household income per year (<4 million yen, 4–6 million yen, 6–8 million yen, 8–10 million yen, >10 million yen, and missing), the age of the youngest child in the household (none; 0–3; 4–6; 7–12;13–15; 16–18; >18), and the number of cohabitants (alone; 2–3; ≥4).

We assessed the psychiatric status of each respondent using validated questionnaires, evaluating them for major depressive disorder (CES-D) [40], obsessive-compulsive disorder (OCI) [41], internet-related problems (CIUS) [42], attention-deficit/hyperactivity disorder (ADHD) (ASRS) [43], autistic spectrum disorder (AQ) [44], social anxiety (LSAS-fear/avoid) [45], general anxiety (STAI-Y-state) [46], and alcohol-related problems (AUDIT) [47]. The nine psychiatric disorders were specifically selected because it has previously been shown that they are affected by the pandemic (see Introduction [7–13]). Details for each questionnaire are in the Supplementary Methods. COVID-19-related items were also measured in surveys during the pandemic [48] (Supplementary Table 1 and Supplementary Methods for details about the survey). First, nine psychiatric scales were selected according to the original purpose to investigate the relationship between smartphone addiction and multiple psychiatric states. Specifically, we selected those that are known to affect internet-related problems (see Supplementary Methods). Some of them were consistent with psychiatric disorders that Caspi [37], who proposed "p factor", mentioned, so we analyzed them for the present study. Others have been reported to worsen in response to stress due to the pandemic e.g., internet addiction, developmental disorders. Therefore, we also included them because they may represent an important aspect of COVID-19 stress-induced changes in mental health.

Statistical analysis

Each psychiatric disorder score at T0 was z-score normalized across subjects. Those at follow-up (T1, T2, and T3) were normalized with respect to the scores at T0. Specifically, the amount of change from the mean at T0 for each score at follow-up was divided by the standard deviation at T0. Next, each normalized psychiatric disorder score (from T0, T1, T2, and T3) from each participant was concatenated across participants. We did so in order to handle not only variability among subjects within each time point, but also a variation of psychiatric states caused by the pandemic simultaneously. Also, by concatenating them, it is expected that results will be less sensitive to accidental outliers at a given time point. Since we had nine types of mental health measures, there are nine columns in total. The number of rows is the number of people multiplied by the number of

time points (4) for each psychiatric disorder score. Correlation among all disorder pairs of concatenated score vectors was calculated to check the covariance of psychiatric status. Then, to extract principal components of multidimensional psychiatric disorders, we performed a principal component analysis (PCA) on the concatenated data. We performed PCA to account for common trends in response to the pandemic across mental disorders. We wanted to know whether it is possible to find the structure of mental disorders, as in previous studies, and whether there are components in it that are contributed by all mental disorders, like the "p factor". If so, we wanted to determine the type of trajectory they follow. Using an orthogonal transformation, a set of correlated dimensions was converted into a set of uncorrelated components [49]. Hence, each principal component (PC) consisted of a set of correlated components of psychiatric disorders, i.e., that covaried overtime during the pandemic. How much each disorder contributed to each PC was numerically indexed as the "loading" of that disorder. The top four PCs explained ~60% of the variance in the data. Accounting for 60% of the total variance is considered acceptable in order to choose the number of components [50]. The nine psychiatric scores of each participant at each time point were then converted into these four PCs, based on the loadings. This analysis was recalculated from data for each condition by sex and age to clarify the robusticity of the data structure for inter-conditions. Changes in scores of each psychiatric disorder and each PC across time points were tested by one-way ANOVA and Tukey's test. Multiple comparisons were adjusted using Bonferroni correction. The adjusted $p < 0.05$ (i.e., unadjusted $p < 0.0056$ in each psychiatric analysis, unadjusted $p < 0.0016$ in each PC analysis) was considered the threshold for statistical significance.

To identify risks and protective factors against exacerbation of each PC, we performed generalized linear model regression (GLM). In each regression model, changes in each component from the baseline for each participant were used as dependent variables. Independent variables included demographics (sex, age, number of cohabitants, marital status, age of youngest child, income, and job type). We specifically asked about the age of the youngest child in the household since it was reported as an important variable explaining exacerbation of mental health during the pandemic [15]. Independent variables also included COVID-19 related variables (income changes, number of received government compensation payments, and changes in daily communication frequency both online and face-to-face, see Supplementary Table 1) and all four PC scores at pre-pandemic (T0). Each PC was used as the dependent variable separately. Model details are provided in Supplementary Methods.

RESULTS

We analyzed data from 2274 study participants who participated in all four surveys. Demographic data of participants are provided in Table 1. Characteristics of the survey population ($N = 3935$, which includes participants who did not complete all four surveys, are described in Supplementary Table 2. Correlation matrices for changes in scores of psychiatric disorders over time are shown in Supplementary Fig. 1. Half (18/36) of all combinations had relatively strong positive (>0.5) or negative (< −0.5) correlations.

Table 1. Characteristics of study population ($N = 2274$).

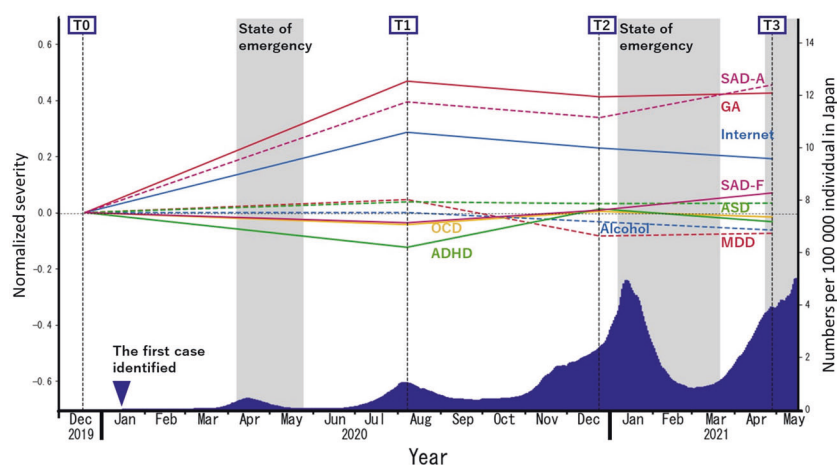| All	2274 (100%)						
Sex	Male	Female					
	1225 (54%)	1049 (46%)					
Marital status	Not married	Married					
	801 (35%)	1473 (65%)					
Age of youngest child in the household	No children	0–3	4–6	7–9	10–12	13–15	16–18	19–
	1254 (55%)	160 (7%)	90 (4%)	101 (4%)	106 (5%)	100 (4%)	101 (4%)	362 (16%)
Household income	Lowest	2nd	3rd	4th	Highest	Missing	
	567 (25%)	495 (22%)	409 (18%)	222 (10%)	382 (17%)	199 (9%)	
Job	No job	Self-employed	Employee	Other			
	375 (16%)	517 (23%)	1177 (52%)	205 (9%)			

Fig. 2 Trajectories of psychiatric scores in the study population (N = 2274). The blue area under the curve represents a 15-day moving average of daily new cases of COVID-19 per 100,000 Japanese residents. GA general anxiety as measured with the STAI-Y, SAD-A avoidance aspects of social anxiety disorder as measured using the LSAS-A, Internet internet-related problems as measured with the CIUS, ASD autism as measured with the AQ, SAD-F fear aspects of social anxiety disorder as measured using the LSAS-F, OCD obsessive-compulsive disorder as measured using the OCI, ADHD attention-deficit and hyperactivity disorders as measured with the ASRS, Alcohol alcohol-related problems as measured with the AUDIT, MDD major depressive disorder as measured using the CES-D.

Impact of the pandemic on scores for each psychiatric disorder

During the observation period, we found abrupt, statistically significant exacerbation of general anxiety, avoidance aspects of social anxiety disorder, and internet-related problems (Supplementary Table 3). These disorders showed no remission during the study. A similar, but the nonsignificant pattern was observed for autism spectrum disorder (ASD). The fearful aspect of social anxiety disorder, obsessive-compulsive disorder (OCD), and attention-deficit/hyperactivity disorder (ADHD) showed an initial drop followed by a gradual increase. Major depressive disorder and alcohol-related problems showed an initial increase, followed by a gradual decrease (Fig. 2 and Supplementary Fig. 2).

Principal component analysis of multidimensional psychiatric states

Multidimensional psychiatric time-series data were decomposed into orthogonal principal components. The top four components explained ~60% of the variance (PC1: 24.1%, PC2: 14.3%, PC3: 11.0%, PC4: 10.6%, in total 59.9%), so we analyzed those further. Principal component 1 (PC1) included all psychiatric illnesses. Principal component 2 (PC2) was composed of social anxiety and internet-related problems. Principal component 3 (PC3) consisted mainly of alcohol-related problems. Principal component 4 (PC4) comprised depression, anxiety, and alcohol-related problems (Fig. 3A). Characteristics of each PC loading are shown in Supplementary Table 4 for the study population and in Supplementary Table 5 for the survey population. All but PC3 worsened during the initial phase of the pandemic, followed by further exacerbation (PC2), sustained elevation (PC1), and partial remission (PC4) (Fig. 3B). Despite showing slight remission in later phases (T2, T3), comparable to the initial phase (T1), PC4 remained higher than baseline (T0) throughout the pandemic. PC3 was excluded from further analysis to identify participant risk/protective factors because, throughout the pandemic, it showed no significant changes relative to baseline (T0) (Supplementary Table 6; trajectories of each PC in survey population are shown in Supplementary Fig. 3).

Regression analyses to identify risk and protective factors

Figure 4 shows the results of generalized linear models to identify factors that may exacerbate or alleviate effects of the pandemic on components of each PC. All results are reported with

coefficients ± standard error (SE) and p values (p). In PC1 and PC2, being female represented a significant risk of exacerbation compared to being male ($\beta = 0.32 \pm 0.05$, $p < 0.001$; $\beta = 0.38 \pm 0.04$, $p < 0.001$). Older age was also associated with exacerbation of PC2 ($\beta = 0.07 \pm 0.02$, $p = 0.010$). In PC1 and PC4, the impact of the pandemic on decreased household income was a risk factor ($\beta = 0.08 \pm 0.02$, $p < 0.001$; $\beta = 0.06 \pm 0.02$, $p < 0.007$). On the other hand, in PC2, being self-employed, experiencing changes (both increase and decrease) in face-to-face communication time with family, and decreased online communication time with family were protective factors ($\beta = -0.16 \pm 0.06$, $p = 0.017$; $\beta = -0.14 \pm 0.05$, $p = 0.007$; $\beta = -0.12 \pm 0.05$, $p = 0.034$; $\beta = -0.14 \pm 0.04$, $p = 0.005$) compared to each reference group. Detailed reports of all regression analyses are shown in Supplementary Table 7.

To assess the influence of participants who dropped out of the study before completion, all analyses were also performed in the "survey population", which included individuals with partial data (Fig. 1). Results are consistent with analyses of complete responders, except for the effect of age in PC4 (Supplementary Fig. 4 and Supplementary Table 8).

DISCUSSION

This is the first study to examine multidimensional psychiatric states at multiple time points from before the COVID-19 pandemic to 1 year after the outbreak (T0: December 2019, T1: August 2020, T2: December 2020, T3: April 2021) in a large online population (including participants with missing data: N = 3935, excluding those with missing data: N = 2274). Average psychiatric disorder scores showed different trajectories across disorders while being correlated within participants. As a result, these psychiatric dimensions were aggregated into four major, orthogonal principal components (PCs). PC1, PC2, and PC4 showed distinct exacerbation trajectories, as well as distinct peaks. PC3 showed no significant change during the pandemic.

These PCs are interpreted as a general psychiatric burden, social withdrawal, alcohol-related problems, and depression/anxiety. Most psychiatric disorders contributed to PC1, which may reflect the general psychiatric burden due to the pandemic. PC2 was mainly associated with fear and avoidance aspects of social anxiety, as well as internet-related problems, which may represent symptomatic social withdrawal. Exacerbation of PC2 may result from strategies to prevent the spreading of the infection, such as
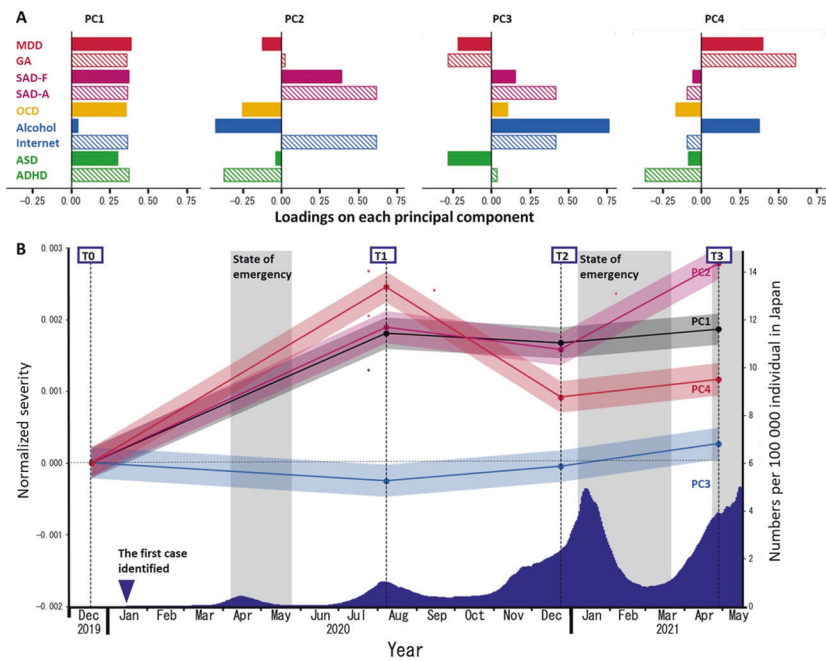
Fig. 3 Trajectories of PC scores obtained from multidimensional psychiatric scores in the study population (N = 2274). A Loadings of psychiatric disorder scores for each principal component. **B** Trajectories of the average of each PC are shown. The blue area under the curve represents a 15-day moving average of daily new COVID-19 cases per 100,000 Japanese residents. Signs of PCs were arranged so that each maximum loading assumed a positive value. Asterisks indicate significant changes in PC score from the previous time point ($p < 0.05$, Bonferroni-corrected). All PC scores during the pandemic (T1, T2, and T3) except those of PC3 are significantly higher than the scores pre-pandemic (T0). MDD major depressive disorder as measured using the CES-D, GA general anxiety as measured with the STAI-Y state, SAD-F fear aspects of social anxiety disorder as measured using the LSAS-F, SAD-A avoidance aspects of social anxiety disorder as measured with the LSAS-A, OCD obsessive-compulsive disorder as measured with the OCI, Alcohol alcohol-related problems as measured with the AUDIT, Internet internet-related problems as measured using the CIUS, ASD autism as measured using the AQ, ADHD attention-deficit and hyperactivity disorders as measured with the ASRS.

social distancing. Repeated avoidance of social activities may gradually instill the notion that social communication is immoral or something to be avoided. Severe social withdrawal—*hikikomori*—has been an increasing social problem in Japan. *Hikikomori* is characterized by a tendency to isolate oneself from society, to stay in one's room, and to become dependent on the internet and games [51, 52]. Internet-related problems and social anxiety are gaining attention as important risk factors for social withdrawal [53–55]. PC4 was mainly associated with depression and anxiety. These PCs peaked at different stages of the pandemic. PC1 and PC4 peaked in the first stage of the pandemic. PC2 peaked with a delay, during the pandemic.

In our analysis, each psychiatric disorder was decomposed into different PCs that evolved along different trajectories. For example, alcohol-related problems contribute significantly to both PC3 and PC4. PC4, a component mainly reflecting depression/anxiety, worsened during the pandemic. PC3, a component mainly reflecting alcohol-related problems, did not change significantly during the pandemic. These data suggest that while alcohol-related problems did not display pandemic-induced changes, some individuals used alcohol maladaptively to cope with depression/anxiety. Moreover, although no clear association with pandemic-related worsening of psychiatric symptoms has been found in a meta-analysis report [16], latent variables of psychiatric disorders may have been adversely affected. In particular, PC1, which is considered like the "*p* factor", and PC2 continue to be worse after T1 compared to T0 and may be affected by the pandemic in the long term. Thus, when assessing changes in mental illness due to the effects of a pandemic, it is important to consider multiple dimensions to identify risks, rather than simply assessing single dimensions.

Our regression analysis further highlighted the importance of flexible countermeasures for mental health problems. Some risk factors were shared across PCs. Specifically, being female was a common risk factor for exacerbation of psychiatric disorders represented by the PCs. Japanese females also experienced a severe increase in suicide during the pandemic, compared with Japanese males [56]. There is an urgent need for counter measures to reduce the physical and mental burdens imposed by the pandemic. In parallel, we identified risks and protective factors that were specific for each PC. General psychiatric burden and depression/anxiety, PC1, and PC4, were strongly influenced by economic factors, whereas social withdrawal, PC2, was strongly influenced by human relationships. The effects of reduced income on mental health are consistent with a previous study reporting individual economic damage as a risk factor for worsening mental well-being during the pandemic [19].

In the social withdrawal component, self-employment and changes in communication were protective factors. Employment in isolation has been associated with higher social isolation during COVID-19 [57], but self-employment may be associated with lower social isolation due to COVID-19. To preserve mental well-being, a successful strategy might involve focusing on countermeasures against economic impact in the early stages of the pandemic, while supporting social interaction may be more important in the later stages of the pandemic.

Given the complex nature of the link between the current pandemic and mental health, this study has some limitations. First, the long-term effects of this pandemic cannot be assessed yet. Second, the psychiatric scores assessed here did not include some important dimensions, such as psychotic symptoms. However, even though the measurements that assess symptoms don't cover
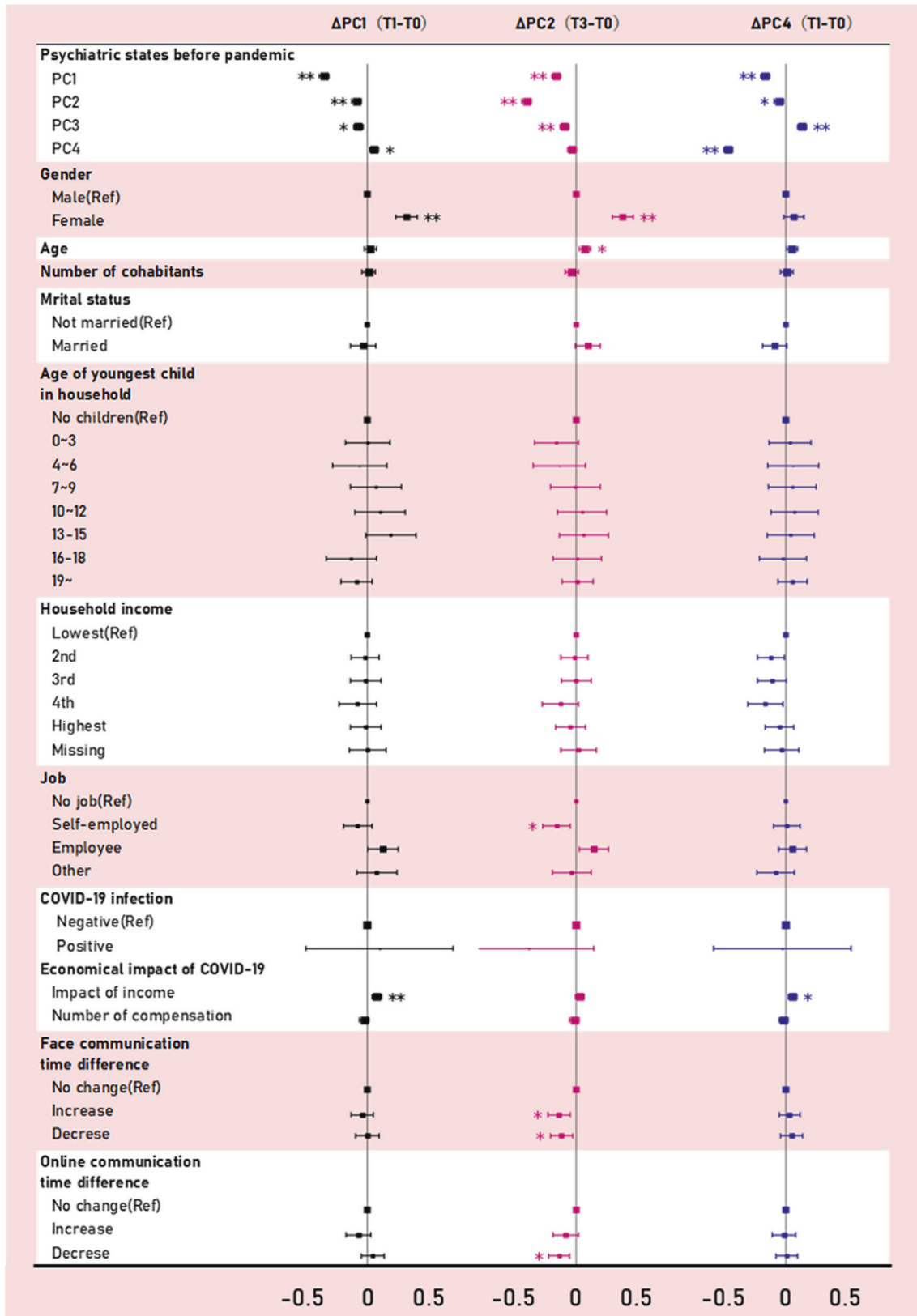
Fig. 4 Fixed-effects regression analyses showing within-person changes in multidimensional psychiatric status during the pandemic. Forest plots show results of fixed-effects regression analyses. Each plot represents standardized beta coefficients with standard errors. Asterisks indicate statistical significance (*p < 0.05, **p < 0.001).

all factors (e.g., internalizing, externalizing, and psychotic symptoms), the general factor of psychopathology is reported to be identifiable [30]. Therefore, we think that we can ignore this problem here. Third, our analysis focused on the Japanese population. Our understanding of the effects of the COVID-19 pandemic on mental health would benefit from international comparisons, including race, culture, religion, and psychiatric states that were not assessed in this study. Fourth, these surveys were conducted using the online recruiting method, and there may be sampling bias. In the generalized linear model analysis, we corrected the confounding factors of age and sex by adjusting them so that the effect of bias can be reduced. As for principal component analysis, it was conducted for each age and sex group, and the results were confirmed to be consistent with the main results (see Supplementary Figs. 5, 6, and 7). Therefore, we conclude that the effect of sampling bias caused by the difference between the general and the study population is limited. Finally, because our data were concatenated across time points, the PCs reflected both temporal covariance and covariance between participants. Future work with more time points may help us clearly distinguish these two effects, to better understand the impact of the pandemic on mental health.

In summary, time courses of nine psychiatric symptoms during the COVID-19 pandemic were aggregated into three exacerbated, orthogonal principal components with different peaks, as well as different modulating factors. Our findings underline the importance of flexible approaches for mental health protection. Long-term monitoring and real-time reporting are both necessary to determine the full consequences of COVID-19 on mental health.

DATA AVAILABILITY

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AUTHOR CONTRIBUTIONS

T.C. made substantial contributions to the study conception and design. T.O., N.K., Y.M., M.H., T.H., and T.C. made substantial contributions to data acquisition. T.O., F.N., T.K., and T.C. conducted statistical analyses. T.O., F.N., T.K., and T.C. made substantial contributions to the interpretation of data. T.O., T.K., F.N., H.T., S.B., T.K., M.N., A.C., M.T., M.K., and T.C. wrote the manuscript. All authors contributed to editing and commenting on the final version. T.C. takes responsibility for the integrity of the work.

COMPETING INTERESTS

N.K, T.H., and M.H. are employees of KDDI Research Inc. Y.M. is an employee of KDDI Corporation. N.K., Y.M., T.H., and M.H. were involved in the study design, data acquisition, statistical analysis, and interpretation of the results. For the remaining authors none were declared conflicts of interest.

ADDITIONAL INFORMATION

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