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Non-randomized controlled trial examining the effects of livestock on motivation and anxiety in patients with chronic psychiatric disorders

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Abstract

Objectives: Patients with chronic schizophrenia exhibit negative symptoms, including decreased work motivation. Animal-assisted therapy programs have been reported to benefit such patients; hence, there is a possibility that sheep-rearing, rather than conventional employment training, may motivate these patients. Therefore, we investigated the effects of a one-day experiential learning program of sheep-rearing on the work motivation and anxiety of patients with chronic schizophrenia.

Methods: Fourteen patients were included in a non-randomized controlled trial conducted between August 2018 and October 2018. The patients' participation in the sheep-rearing experiential learning (one day; intervention day) and normal day care (one day; control day) programs were compared. The salivary cortisol and testosterone levels and State-Trait Anxiety Inventory (STAI) scores of the patients were analyzed.

Results: The patients' salivary testosterone was significantly higher on the intervention day ($p = 0.04$) than on the control day ($p = 0.02$). Their salivary cortisol was lower on the control day than on the intervention day, although the difference was not significant. Regression analysis was performed based on the change in salivary cortisol levels and STAI-Trait scores ($p = 0.006$), and a regression equation was established.

Conclusions: The study revealed that participation in sheep-rearing may have promoted the testosterone production but did not increase anxiety in patients with schizophrenia. Additionally, regression equations for salivary cortisol levels in such patients may provide information on individual differences in anxiety levels.

Keywords

Anxiety, motivation, non-randomized controlled trial, schizophrenia, rehabilitation, social support

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Introduction

In Japan, increased support is being sought for the discharge of long-term hospitalized patients with mental illness; however, their reintegration into society has been slow. Moreover, the harmful effects of long-term hospitalization include patients' inability to adapt socially; hence, there are limited employment opportunities available to them and, additionally, they may find work stressful. Therefore, they experience isolation from society, difficulties in day-to-day living, and psychological distress.[1,2] Cognitive dysfunction strongly influences the social outcomes of schizophrenia and its negative symptoms, including decreased motivation ("inaction"), decreased spontaneous speech, and social withdrawal ("autism"), and is involved in the social prognosis of these patients.

In Japan, the agricultural working population is aging; the number of workers has decreased by approximately half in the past 20 years.[3] Furthermore, it is difficult for people with

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disabilities (on welfare) to find employment with adequate wages, despite their willingness to work.[3] "Agricultural welfare cooperation" connects "agriculture, which has insufficient man-power" to the "people seeking to secure employment and improve wages," thereby bridging the existing gap.

A survey conducted by the Cabinet Office of Japan in 2018 revealed that many people with mental disorders are "isolated" from society, are "withdrawn" at home, and have limited contact with their families or local communities.[4] In addition, the duration of hospitalization for these patients has become a problem worldwide.[5] In most Organization for Economic Co-operation and Development (OECD) countries, "deinstitutionalization" is a way-forward approach in healthcare transition from hospitals to communities. Japan's progress in deinstitutionalization has been slow, and it still has the highest number of psychiatric beds among the OECD countries, with 269 beds per 100,000 people, while the global average is 68 per 100,000.[5]

However, interventional programs for improving mental health and preventing mental disorders differ between countries and across age-groups. In particular, patients with chronic schizophrenia, which is a common disorder among long-term hospitalized patients in Japan, show negative symptoms such as decreased motivation and easy fatiguability, which hinders their reintegration into society.[2]

Schizophrenia has a pubertal onset and causes dramatic and lifelong impairment in social and occupational functions.[6] It is characterized by negative symptoms such as decreased motivation, decreased spontaneous speech, and social withdrawal; positive symptoms such as delusions and hallucinations; and cognitive symptoms such as impaired speech, attention, and thinking, resulting in impaired communication skills.[2]

Barch suggested that schizophrenia decreases motivation and motility due to dopamine dysfunction.[7] It is considered that there is a deficiency in the involvement of the prefrontal cortical reward system (cortical-striatal system function) in cognitive control, which causes a decline in goal-oriented behavior.[7] Shirayama et al.[8] observed a negative correlation with testosterone levels and a positive correlation with cortisol ($p < 0.01$) levels in patients with schizophrenia who had "moderately but not low negative symptoms." Negative symptoms are major factors in patients with chronic schizophrenia.

Multiple studies support the relationship between sex hormones and the development and course of schizophrenia. Low endogenous testosterone levels are associated with increased negative symptoms,[8–12] worse cognition,[13] and impaired emotion processing[14,15] in men with schizophrenia. A clinical trial reported that testosterone augmentation ameliorated negative symptoms in men with schizophrenia.[15] These studies suggest that a deficit in circulating testosterone or brain response to testosterone may be related to functional impairments. The interaction between psychological stress and immune system has been associated with cognitive impairment in schizophrenia.[16,17] Havelka et al.[17] compared cognitive function (memory, attention, psychomotor, verbal fluency, and executive function) test results and cortisol levels in patients with schizophrenia. It was reported that high afternoon cortisol levels were significantly associated with impaired memory function.

Recent studies state that animal-assisted therapy (AAT) programs may benefit the patients receiving treatment for schizophrenia.[18–20] The suggested benefits are focused on self-esteem, self-determination, positive and emotional symptoms, anhedonia, and effects on day-to-day living.[20–22]

However, these programs were carried out under certain conditions as part of therapy or rehabilitation, and most of the evaluation indicators focused on the stability of the symptoms.[23] It was not an evaluation of whether AAT will lead to the employment of patients with schizophrenia, who live in the local community. It was also important to observe whether it was linked to employment and the existence of anxiety and motivation. To the best of our knowledge, previous studies reporting the effects of AAT on patients with schizophrenia did not include indicators of AAT and testosterone (motivation).[23]

Therefore, this study aimed to implement a livestock-based business development project in collaboration with Agricultural Fortune (Ishikawa Lamb), and evaluate the future employment possibilities for patients with schizophrenia. This project incorporates the operational process of the sheep-rearing business, from breeding to meat processing, into the employment support activities conducted at welfare establishments, and provides experiential learning on sheep-rearing to patients with mental disorders. This study includes a preliminary survey conducted to examine the effect of a one-day sheep-rearing experiential learning program on the work motivation and anxiety of people with chronic schizophrenia.

We investigated patients' testosterone and cortisol levels, and their State-Trait Anxiety Inventory (STAI) scores,[24] since these were reported to be associated with the onset of negative symptoms that hinder the reintegration of patients with schizophrenia into society. Additionally, we focused on trait and state anxiety in patients with chronic schizophrenia and compared the effect of the experiential learning program to occupational therapy on the context of normal psychiatric day care activities.

Methods

The study

Sample. All subjects who met the following criteria were invited by poster to participate in a one-day sheep-rearing experiential learning program after ethical review approval, and those who agreed to participate in the study were considered as participants.

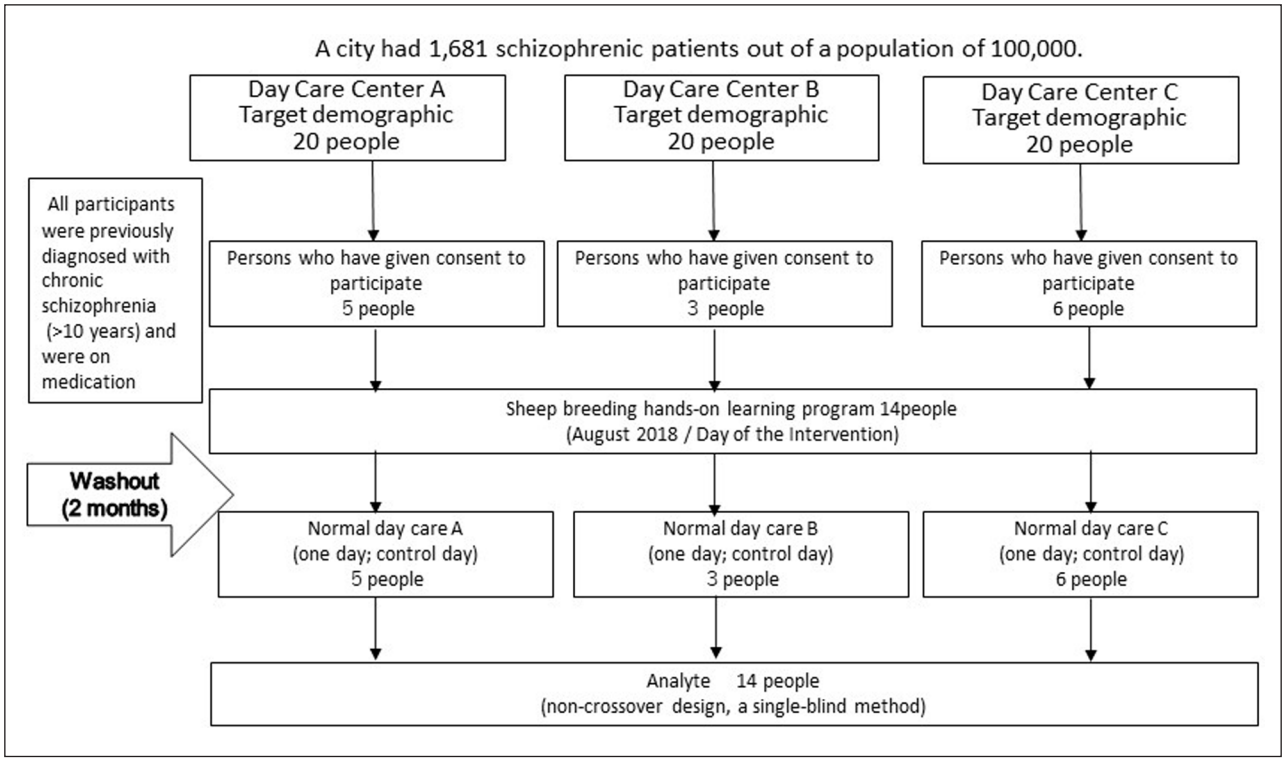

Figure 1. Study timeline.

- Patients were diagnosed with schizophrenia according to the revised fourth edition of the Diagnostic and Statistical Manual of Mental Disorders. (DSM-IV-TR[25]).
- Patients who had survived for more than 10 years since the onset of schizophrenia and whose symptoms indicated a chronic phase.
- Patients who are aspiring to work.
- Patients who are attending psychiatric day care or receiving employment support facilities for persons with disabilities.
- Patients who consented to participate in this program based on their doctor's recommendation.
- The exclusion criteria were as follows:
- Patients who are allergic to animals.
- Patients who reacted negatively to animals.

A total of 60 potential participants were identified (20 in each of the 3 facilities). Among them, 18 expressed an interest; however, only 14 consented to participate in it. The required sample size was 35 participants with an effect size of 0.8 (G*Power 3.1 , Heinrich Heine University, Dusseldorf, Germany). Since this study included 14 participants; the effect size was calculated at 0.3, therefore, it was rather small. All participants received rehabilitation and daily life training twice a week with the support of occupational therapists, nurses, and psychiatric social workers in the day care facility program of their respective psychiatric hospital. The number of patients with schizophrenia (during hospital visits) in a certain city was 1681 out of a population of 100,000 (Ministry of Health, Labor and Welfare Patient Survey 2017).

Design. This study considered a non-randomized controlled trial. A single-blind method was used, in which participants do not know in which group would be the intervention. Written Informed Consent was obtained from all the subjects involved and they had decisional capacity to provide a written Informed Consent. The study period extended from August 2018 to October 2018. The participants' response to the sheep-rearing experiential learning (one day; intervention day) and normal day care (one day; control day) programs were compared. The survey was conducted on both days from 10:00 to 10:30 am (before the program) and from 3:00 to 3:30 pm (after the program). Since no effect of the intervention was observed based on the intervention and control days, the study was performed with a washout period of 2 months (Figure 1).

Method. The activity started at 8:30 am on both days. We arrived at the experience site by bus on the intervention day and initiated the experiential learning program at 10:30 am (Figure 2). The main activities included feeding and herding the sheep and cleaning the sheep-pens in the facility. On the control day, the participants gathered at the venue by 8:30 am, communicated with each other, performed morning exercises, and health checks were conducted. Exercise and occupational therapy were performed in the morning and

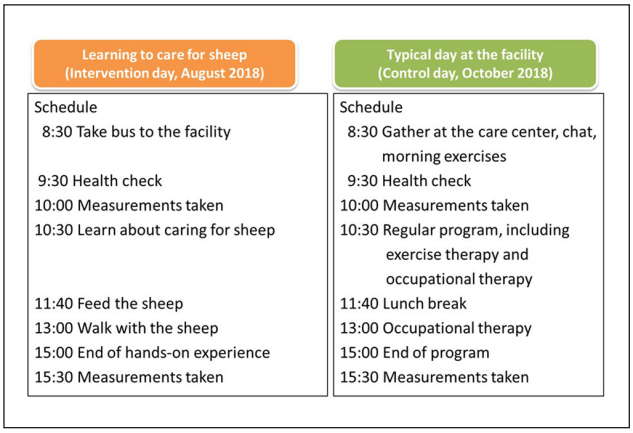

Figure 2. Intervention protocol.

afternoon (Figure 2). The activity end time was 3:00 pm on both days. Significant diurnal fluctuation in the salivary cortisol and testosterone was reported; they increase during sleep, are the highest in the early morning, and decrease thereafter with daytime activity.[26,27] The survey responses and saliva were collected twice, at 10:00 am and 3:00 pm. All participants were assigned an employment support staff-in-charge. The workload was equally distributed, and work was allocated without any bias.

All participants took their medications in the morning and at night or once in the morning, but they did not take any medication during activity hours.

The three variables measured were patients' cortisol and testosterone levels in saliva and the STAI scores. Cortisol is a steroid hormone that increases acute psychological and physiological stress and affects the metabolic, immune, vascular, and central nervous systems[28]; hence, it is vital for an individual's psychological and physical health. Salivary cortisol concentration has been reported to increase by 50%–100% during instances of acute psychological stress such as delivering a speech.[29] Testosterone is a steroid hormone. Salivary testosterone is hypothesized to reflect free testosterone level in blood. The correlation between testosterone in blood and saliva is not necessarily high,[30] possibly due to changes in sex hormone-binding globulin. STAI was proposed by Spielberger et al.,[24] and a Japanese version was designed by Nakazato and Mizuguchi.[31] It is used in clinical settings to diagnose anxiety and differentiate it from depressive syndromes. Additionally, it is often used as an indicator of caregiver distress.[31,32] STAI has 20 items each for evaluating trait and state anxiety. All items are rated on a four-point scale (e.g., from "almost none" to "almost always"). The STAI criteria were as follows: A-State III (normal) 32–40 points for men and 31–41 points for women, and IV (high) 41–49 points for men and 42–50 points for women; A-Trait, III (general) 33–43 points for men and 34–44 points for women, and high 44–52 points for men and 45–54 points for women. The tendency toward experiencing anxiety was stronger for a higher score.[24]

Measurement. Participants were provided with an explanation for saliva collection before conducting the procedure. Thirty minutes prior to the collection, the participants were not allowed to smoke, eat, or exercise and, during the procedure, an instructor was assigned to guide them and confirm that the precautions were followed. A special saliva collection sponge (Salivette®, Sarstedt, Germany) was used .[33] The mouth was lightly rinsed with water and the sponge was placed in it; patients were asked to thoroughly chew it for 2 min to soak up the saliva. STAI was self-administered simultaneously.

The sponge was placed in a tube and centrifuged (20°C, 3000 rpm, 1.5 mL of the supernatant (1 min, 10 min)); subsequently, it was removed and frozen at −20°C. Cortisol and testosterone present in the saliva sample were quantified and measured by the Environmental Impact Assessment method (Institution SRL, Inc., Tokyo).

Analysis. Wilcoxon's test was used to compare the salivary cortisol and testosterone levels as well as the STAI scores recorded before and after the program. The differences observed in the parameters before and after each intervention program on both days were compared. The salivary cortisol and testosterone levels and STAI scores were analyzed and intergroup comparisons were performed using the Mann-Whitney *U*-test. To examine the relationship between the changes in salivary cortisol levels and STAI scores before and after the intervention, their correlation was calculated, and the regression equation was examined. IBM SPSS 25 for Windows was used for all statistical processing, and the significance level was set to 5%.

Ethics. This study was approved by the Ishikawa Prefectural Nursing University Ethics Committee (Kan-Dai No. 865). The purpose, outline, and ethical considerations of the research were explained orally and in writing to the director of the research cooperation institution, and consent was obtained. Subsequently, the patients and facility staff were informed of the research purpose and outline. They were assured that there would be no disadvantages for non-participation; anonymity was ensured, and strict data management was guaranteed. Individuals who provided written consent were included in the study. The trial registration number is UMIN000050224.

Results

Characteristics of the participants with chronic schizophrenia

Of the 14 participants observed, 5, 3, and 6 were from facilities A, B, and C, respectively (8 men, mean age 56 ± 13.79 years (30–72 years)). All participants were previously diagnosed with chronic schizophrenia (>10 years) and were on medication (Table 1); there was no change in prescription medication during the study period. All the patients

Table 1. Demographic data of the study participants.

S. no.	Name of illness	Medication	Age	Sex	History of illness (year)
1	Schizophrenia	Risperidone	60	Male	25
2	Schizophrenia	Risperidone	46	Male	20
3	Schizophrenia	Bronanserin	72	Male	35
4	Schizophrenia	Zeplion, Abilify	39	Female	19
5	Schizophrenia	Risperidone, Olanzapine	67	Male	30
6	Schizophrenia	Aripiprazole	30	Female	10
7	Schizophrenia	Lithium Carbonate, Sodium Valproate, Risperidone, Lodopin	37	Male	15
8	Schizophrenia	Risperidone	67	Male	30
9	Schizophrenia	Olanzapine, Levomepromazine Maleate, Zeplion	68	Male	32
10	Schizophrenia	Risperidone	62	Male	40
11	Schizophrenia	Risperidone	68	Male	42
12	Schizophrenia	Zeplion, Abilify	70	Female	35
13	Schizophrenia	Risperidone, Olanzapine	51	Female	25
14	Schizophrenia	Risperidone	46	Female	30

were unemployed (7 had no prior employment experience or history) and attended psychiatric day care and community activity support centers twice a week; they actively participated in the daily activities and employment training through occupational and exercise therapy. Decrease in the motivation to either start or continue with work is a cause for unemployment, and this is not unusual among individuals with chronic schizophrenia.

Comparison of changes observed before and after the intervention program (intra-group comparison)

To compare the changes observed before and after the intervention program, the respective measured values of cortisol and testosterone in saliva and STAI were examined by Wilcoxon signed-rank test on the intervention and control days. Salivary testosterone significantly increased on the intervention day ($p=0.04$) and significantly decreased on the control day ($p=0.02$; Table 2). Salivary cortisol levels did not change significantly on the intervention day; however, it significantly decreased on the control day. STAI scores decreased on both days after the intervention program; however, the change was insignificant. Participants demonstrated IV (high) level anxiety on both days (Table 2).

Comparison by different intervention programs (comparison between groups)

To compare the changes observed among the participants between the intervention and control days, salivary cortisol and testosterone levels, and STAI scores before and after intervention, the observations were analyzed using the Mann-Whitney *U* test. Salivary testosterone levels significantly improved after the intervention day and were higher than that on the control day. No significant changes were found in patients' salivary cortisol or STAI scores due to different interventions (Table 2).

Examination of the relationship between changes in salivary testosterone and cortisol levels and changes in STAI scores before and after the intervention

The changes in salivary testosterone and cortisol levels and changes in the anxiety scale between both days were analyzed to investigate the correlation between them. A significant correlation was found between the change in salivary cortisol levels and STAI A-Trait (Figure 3, $p=0.003$, $r=0.690$). However, no significant correlation was found between the STAI A-state, salivary testosterone, and age. Therefore, a regression analysis was performed, with the amount of change in cortisol levels in saliva as the dependent variable and the amount of change in STAI A-Trait scores as the explanatory variable, to investigate their mutual relationship with a significance level of 5% or less ($p=0.006$; Table 3). The following regression equation was established:

$$\left[\text{y: cortisollevels in saliva}\right] = 0.008 \times \left[\text{x: A-Trait}\right] - 0.023;\ R^2 = 0.423.$$

Discussion

Working and motivation in chronic schizophrenia

Cognitive dysfunction begins in adolescence. It strongly influences the social outcome of schizophrenia and the patient's social prognosis along with the emergence of negative symptoms such as "inaction/autism" and withdrawal. Schizophrenia causes dramatic and lifelong disabilities in physical and professional functioning.[6] All the participants in

Table 2. Comparison before and after the intervention program.

	Day of the intervention ($n = 14$)		p-Value[a]	Effect size (r)	p-Value[b]	Effect size (r)
Measurement items	Before intervention	After intervention				
Testosterone level in saliva						
M (ng/mL) ± SD	0.146 ± 0.011	0.224 ± 0.076	0.041*	−0.650	0.003**	−0.720
Min–Max	0.110–0.220	0.220–0.680				
Cortisol levels in saliva						
M (μg/dL) ± SD	0.238 ± 0.035	0.199 ± 0.027	0.173	−0.460	0.199	−0.300
Min–Max	0.130–0.460	0.090–0.420				
Anxiety trait						
M ± SD	45.333 ± 3.675	44.000 ± 2.437	0.324	−0.290	0.370	−0.190
Anxiety state						
M ± SD	40.750 ± 3.983	35.667 ± 2.372	0.100	−0.460	0.198	−0.230
Min–Max	23.000–69.000	23.000–55.000				
	Day of control ($n = 14$)		p-Value[a]	Effect size (r)		
	Before intervention	After intervention				
Testosterone level in saliva						
M (ng/mL) ± SD	0.154 ± 0.007	0.134 ± 0.007	0.016*	−0.730		
Min–Max	0.120–0.200	0.090–0.170				
Cortisol level in saliva						
M (μg/dL) ± SD	0.260 ± 0.032	0.173 ± 0.011	0.021*	−0.770		
Min–Max	0.150–0.470	0.100–0.260				
Anxiety trait						
M ± SD	46.636 ± 2.103	42.546 ± 2.674	0.114	−0.500		
Min–Max	38.000–62.000	28.000–63.000				
Anxiety state						
M ± SD	40.000 ± 3.751	41.182 ± 3.086	0.358	−0.290		
Min–Max	26.000–65.000	28.000–61.000				

[a]Wilcoxon Signed-Rank test (Comparison before and after the intervention within the same group).
[b]Mann-Whitney U test (Comparison difference before and after the intervention).
*$p < 0.05$. **$p < 0.01$.

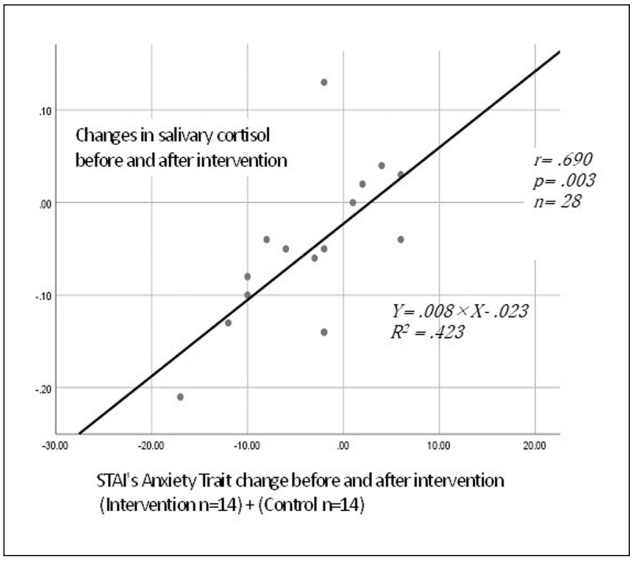

Figure 3. Relationship between the STAI's anxiety trait score and salivary cortisol change (scatter plot and regression line).

this study lived in the community and were unemployed. This is not unusual among patients with chronic schizophrenia because decreased motivation is related to unemployment.

Impact of the sheep-rearing experiential learning program

Comparison of the changes in patients' salivary cortisol and testosterone levels as well as the STAI scores observed before and after the sheep-rearing experiential learning and the usual day care programs were conducted revealed that salivary testosterone increased on the intervention day and decreased on the control day. Thus, the one-day sheep-rearing program may have promoted patients' testosterone production. Testosterone is associated with physical stress in healthy men[34]; Vercammen et al.[15] reported that testosterone fluctuations within the normal range did not significantly affect emotional or cognitive processing in men without schizophrenia, even though they are correlated. A higher endogenous testosterone level is associated with improved

Table 3. Relationship between STAI's anxiety trait and salivary cortisol level change (multiple regression analysis stepwise).

Independent variables	Age	Testosterone	Cortisol	A-Trait	A-State	SD	*M*
Age							
r	—	−0.115	0.027	0.030	0.101	56.417	14.646
p	—	0.660	0.915	0.893	0.654		
Testosterone							
r		—	0.312	0.269	−0.258	0.024	0.129
p		—	0.278	0.333	0.354		
Cortisol							
r			—	0.690**	0.094	−0.059	0.082
p			—	0.003	0.728		
A-Trait							
R				—	0.329	−3.348	9.345
P				—	0.125		
A-State							
R					—	−3.000	12.696
P					—		

Cortisol = 0.008 × A-trait-0.023. $R^2 = 0.423$.
**$p < 0.01$.

behavioral performance and decreased brain activation in men with ataxia.[15] In the present study, some participants actively communicated with positive comments such as "fun," "good to participate," and "interesting" after the intervention day.

Sheep are social animals that can recognize and approach familiar human faces, unlike other farm livestock such as cows, pigs, and hens.[35] The act of approaching and feeding the sheep, and the sheep subsequently returning for feeding, may have led to emotional empathy and attachment formation, similar to what is experienced with pets. Previous studies of AAT have reported that intervention with dogs increased the amount of conversation and social activity in nursing homes.[36] Studies confirming the therapeutic effect of intervention therapy have reported that AAT reduced stress during the sessions.[37] Hence, it is possible that animal–human interaction has a positive effect on the patients. Canine-mediated therapy is effective in improving verbal and non-verbal communication in patients with intellectual disabilities,[38] and this may be useful for improving verbal and emotional expressions involving higher brain functions. Dogs are social animals that recognize human faces[39]; similarly, sheep can recognize human faces, leading to an improved non-verbal communication among people with intellectual disabilities. This may have affected changes in the salivary testosterone levels.

However, the differences in the groups observed in this study (Figures 1 and 2) suggest that small variations in testosterone levels, within the normal range, do not impact emotional and cognitive processing in healthy men; however, they can influence brain activity and behavior in patients with schizophrenia.

On the other hand, of the five female participants (35.7%) in this study, two were in their 30s, and the rest were postmenopausal women. In a previous study by Braunstein et al.,[40] the effects of testosterone in women, mean, median, and weighted mean hormone levels were determined throughout the phases of the menstrual cycle, along with percentiles, representing women in their 30s. The results showed that healthy women (aged 18–49 years) with normal menstrual cycles had limited amounts of testosterone (i.e., one-tenth of the amount in men). The study reported that the overall fluctuation in elevated testosterone in the mid-menstrual period is small. In addition, our study was a comparative study that explored the amount of change in the same person before and after the intervention on the same day, so the effects of menstruation and sex differences were unlikely. Although it is believed that testosterone declines with age in both men and women, which leads to menopause,[40] the fact that the sheep breeding intervention in this study resulted in an improvement in testosterone is a significant achievement.

Conversely, salivary cortisol did not show a significant change on the intervention day; however, a significant decrease was seen on the control day. This is likely because the participants did the work they were accustomed to on the control day and, hence, were unstressed. However, the difference between the groups due to the intervention was not significant. Therefore, not all participants were able to work comfortably on the control day as compared to the intervention day.

Previous studies have reported that salivary cortisol level decreases during AAT sessions in patients with other types of psychological disorders, such as children with autism,[41] and men with insecure attachment disorders.[42] A study of patients undergoing treatment for schizophrenia did not report changes in cortisol levels following patients' interaction with animals.[43] Calvo et al.[23] assessed the effects of

an AAT program as an adjunct to a conventional 6-month psychosocial rehabilitation program for patients with schizophrenia. The results revealed a significant decrease in cortisol; however, the change in the salivary alpha-amylase level was not significant.

Sample collection was reportedly not always successful due to the influence of medications taken by patients with schizophrenia and their lack of understanding of the saliva collection procedure; approximately 17% of the collected samples were not used as they were inadequate sample volumes for analysis.[23] Additionally, the need to extend and optimize the extraction and analysis of saliva samples were reported.[23] In the present study, detailed instructions, such as avoiding smoking or eating 30 min before the procedure, oral rinsing with water, and chewing the saliva collection sponge several times to ensure successful saliva extraction, were provided; hence, an adequate amount of saliva was obtained and its effects were appropriately analyzed. However, this procedure does not always ensure extraction of an adequate amount of saliva under the influence of medication; hence, a method to immediately and continuously quantify and measure blood cortisol levels is needed.[16] Therefore, increasing the number of N (i.e., number of intervention sessions) in the equation of STAI (Figure 3) is necessary to use it as an equation for estimating the cortisol levels in patients with chronic schizophrenia.

The mere presence of a dog in a therapy session may improve adherence, especially when a patient with schizophrenia successfully bonds with the dog; this effect needs to be further investigated.[23] We have previously reported that people with intellectual disabilities demonstrated improved frontal lobe function and blood flow,[1] and a positive attitude toward agricultural work following sheep-rearing for 5 days a week, for 5 months. This suggested that sheep-rearing may have activated the frontal lobe function and motivated the participant. Hence, a sense of responsibility and accomplishment in working as a livestock breeder may have stimulated the participant's motivation more than in the case of AAT as a therapeutic intervention. Since sheep-rearing can generate income, continuation of the program is necessary to examine its therapeutic and economic effects on patients with schizophrenia.

Relationship between specific anxiety in patients with chronic schizophrenia and salivary cortisol levels

A significant correlation was found between the change in salivary cortisol levels and STAI A-trait; consequently, accordingly, a regression analysis was performed. Thus, anxiety can be measured via salivary cortisol levels.

STAI describes anxiety as A-state (a measure of the current state of anxiety in an individual) and A-trait (an individual's tendency to be anxious when stressed). It is divided into scales to predict the anxiety levels.[24] Long-term anxiety is a characteristic of schizophrenia; however, since a strong correlation with the salivary cortisol level of participants with chronic schizophrenia was observed, this level needs to be measured. Therefore, predicting the stress-related anxiety levels of an individual may be possible. Additionally, this could predict uncertain behavior when unpredictable events occur in work or daily life or during changes in conditions such as the relapse of symptoms, decreased motivation, and interpersonal conflicts.

The interaction between psychological stress and the immune system has been reported to be related to cognitive deficits in schizophrenia.[44]A machine-learning algorithm was used to examine the pattern of stress and immune network associated with cognitive deficits in chronic schizophrenia; it revealed that these patients demonstrated dysfunctional responses to psychological stress.[44] Havelka et al.[17] tested cognitive functioning (memory, attention, psychomotor, verbal fluency, and executive functions) in patients with schizophrenia, after symptom alleviation, using a neurocognitive test battery and revealed that higher afternoon cortisol levels at the initiation of treatment were significantly associated with impaired memory functions. In a comparative study of cognitive functioning and stressors in 37 patients with chronic schizophrenia and 35 age- and gender-matched healthy controls, a multiple stepwise linear regression analysis revealed that positive and negative syndrome scale cognitive sub scores were significantly associated with the duration of illness and cortisol × tumor necrosis factor-alpha × interleukin-8.[44]

A study of stress-related cortisol responses in depression[27] reported that supranormal cortisol responses in sociophobic individuals may be negatively associated with general social function than in a healthy population with unimpaired social function.[45]

In the present study, participants' cortisol levels were slightly higher (mean: 0.26 mol/L, range: 13.0–46.0) than that of a healthy young male population (median: 0.19 mol/L).[46] However, after the intervention, there was a significant decrease in both groups.

In the stress vulnerability model of patients with schizophrenia presented by Zubin et al.,[47] the combination of psychosocial stress and vulnerability (information processing disorders, premorbid personality, and personality traits) increased patients arousal and emotional levels. Psychiatric symptoms appear when stress exceeds a person's coping ability; therefore, for patients with chronic schizophrenia, involvement in society and working is extremely stressful. Adaptability is affected due to stress vulnerability, anxiety, hesitation, and conflict arising from the decision to move to a new environment. Prediction of trait anxiety via salivary cortisol level assessment could enable professionals to provide support before a patient's stress level exceeds the threshold value that they can withstand in situations such as employment training and interpersonal relationships. Hence, a device to measure the salivary cortisol levels that provides immediate results is needed.

The participants who heightened their anxiety by volunteering for the sheep-rearing program demonstrated a decrease in state anxiety post-experience; however, their trait anxiety did not decrease. Comparatively, in normal work activities, high specific anxiety was observed at the time of participation; however, it decreased toward the end. This could have brought about stability in the personality tendency of anxiety and is important for continuing employment. Therefore, in the future, the participants' anxiety can be immediately determined by measuring their salivary cortisol levels, and they can switch to work, which decreases their anxiety when needed. It may be used as an indicator to support continued employment and to immediately respond to interpersonal stress.

Limitations

First, the results of this study may be biased because of the small sample size and a non-random sampling method. Hence, the number of participants needs to be increased for improved generalization of the results. Second, it was difficult to establish a control group consisting of chronic schizophrenic patients with the same symptoms as the intervention group. In addition, to study the effect of the intervention, it was not appropriate to set up a control group consisting of healthy people. Furthermore, it was difficult to obtain the consent of patients with acute schizophrenia to participate in the study and make them understand the details; additionally, appropriate treatment needs to be prioritized in order to use them as controls. Therefore, the present study used a non-crossover design in which the same subjects were divided into an intervention and a control period. In order to avoid the influence of the intervention, a 3-month interval was set between the intervention and control periods. However, to accurately determine the effectiveness of this study, another person with the same disease should be set up as a control group, or in a crossover design, and the experiment should be conducted. An increase in the number of co-researchers may facilitate the use of random sampling methods. Therefore, we would like to work with welfare facilities for people with disabilities and livestock farmers to further validate the results of this study. Third, at the time the participants were diagnosed, the main diagnostic criteria in Japan were DSM-IV/CDI-10. Therefore, we adopted the DSM-IV criteria for diagnosing the mental disorders of participants, rather than the current up-to-date DSM-V diagnostic criteria. Therefore, there exists a possibility of error in participants' diagnoses due to the current criteria. In particular, the possibility of other psychiatric disorders (such as temporal lobe epilepsy, frontal brain tumor, auto-immune encephalitis, cocaine abuse, hyperthyroidism, pellagra, Fahr's disease and Wilson's disease) cannot be ruled out. Finally, we used salivary cortisol and STAI as the measures of anxiety for the participants in the present study. Future research should include neuropsychological tests and personality assessments when measuring the neuropsychiatric effects of sheep-rearing as a form of psychiatric rehabilitation. Finally, we used salivary cortisol and STAI as the measures of anxiety for the participants in the present study. Future research should include neuropsychological tests and personality assessments when measuring the neuropsychiatric effects of sheep-rearing as a form of psychiatric rehabilitation.

Conclusion

We have implemented the first agricultural and fortune cooperation (Ishikawa Lamb) livestock-based business development project in Ishikawa Prefecture and evaluated its outcomes and future possibilities. We have investigated the effects of a one-day sheep-rearing experiential learning program on the work motivation and anxiety of patients with chronic schizophrenia. Previous studies have reported that testosterone and cortisol levels and STAI scores are associated with the onset of negative symptoms, including decreased motivation and cognitive function, which hinder the reintegration of these patients into society. The results of a comparative study on the effects of sheep-rearing experience versus work therapy on normal day care activities (focusing on trait and state anxiety) revealed the following: (a) participation in the one-day sheep-rearing program may have promoted testosterone production in the participants; (b) salivary cortisol level was stable in both the intervention and control groups, and the experiential learning program did not increase anxiety, which is related to stress vulnerability, among patients with schizophrenia. The salivary cortisol level assessment in patients with chronic schizophrenia may provide information on individual differences in personality traits that tend to cause anxiety or those that are relatively stable.

Based on the results, we propose that the sheep-rearing experiential learning program can be a viable rehabilitation approach for patients with chronic schizophrenia. Anxiety may be predicted at an early stage using a simple and non-invasive physiological index to aid in the continuation of employment for these patients. We are planning to increase the number of participants and extend this research to improve the employment opportunities of patients with chronic schizophrenia, motivate their engagement in social activities and participation, and develop and sustain interest in the livestock industry.

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Author contributions

NS and MI conceived and designed the study. NS, SO, and CY performed analysis and interpreted the data. KA, NS, and CY executed the data collection and research work. NS drafted the manuscript. SO and MI reviewed the statistical analysis, and reviewed and edited the draft manuscript. All authors reviewed and approved the final version of the manuscript.

Declaration of conflicting interests

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Informed consent

The research subjects were those who were able to clearly express their willingness to participate in the study on their own, and who were able to understand and respond to the content of the tests and questionnaires administered by the researchers. The research was conducted only after ensuring that the participants had understood the purpose and content of the research and had given their consent. Written Informed Consent was obtained from all the subjects involved and they had decisional capacity to provide a written Informed Consent.

Trial registration

The trial registration number is UMIN000050224.

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Availability of data and material

The research data set is available upon request from the corresponding author.

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