Treating Agitation in Patients with Dementia with a Therapy Dog in a Milieu Therapy Setting on a Geropsychiatric Ward

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Abstract
Background: Animal-assisted intervention has become a common therapeutic practice used for patients with dementia in home-dwelling and institutions. The most established procedure is a visiting service by specially trained dogs and their owners to improve social interactions and reduce symptoms of agitation. Objectives: The study aims to investigate the effects of a therapy dog on agitation of inpatients with dementia in a gerontopsychiatric ward. Materials and Methods: The severity of agitation was assessed by a rater blinded for the presence of the dog via the Overt Agitation Severity Scale (OASS). The scale was conducted on 1 day with the dog and his handler present (resident doctor on the ward) and on another day with only the handler present. Each patient was his/her own control. Heart rate variability (HRV) and serum level of brain-derived neurotrophic factor (BDNF) of the patients were measured on both days. 26 patients with the Mini-Mental Status Examination (MMSE) score <21 and the diagnosis of dementia were included in the study. Results: A significant reduction of agitation in the OASS could be shown when the dog was present (p = 0.006). The data neither demonstrated a difference in the HRV for the parameters mean heart rate (p = 0.65), root mean square of successive differences (p = 0.63), and high frequencies (p = 0.27) nor in serum BDNF concentrations (p = 0.42). Discussion: Therapy dogs can be implemented as a therapeutic tool in a gerontopsychiatric ward to reduce symptoms of agitation in patients with dementia. The study was registered in the German Clinical Trials Register (DRKS00024093).

Introduction

Worldwide established care systems are being burdened by the increasing incidence of dementia resulting from the demographic change in society. A meta-analysis of international studies estimates that 5–8% of the population over 60 years suffers from dementia [1, 2]. The lack of causal treatment options for most neurodegenerative diseases renders the development of complementary interventions essential to reduce the distress not only of the
patients but also of the caregivers and relatives. With progression of the disease, those are often confronted with challenging patient behavior like agitation, psychomotor restlessness, anxiety, and aggression. In the Cardiovascular Health Study, Lyketsos et al. [3] detected, next to apathy and depression, agitation as the most frequent neuropsychiatric symptom in patients with dementia. According to Afram et al. [4], these neuropsychiatric symptoms are the most common cause (25%) for admission into a nursing home. A study in a Canadian nursing home calculated an expenditure of 30 USD per month with each additional point in the “Neuropsychiatric Inventory” [5]. The treatment of neuropsychiatric symptoms with psychopharmaceuticals is often limited by low-effect levels [6], side effects, comorbidities, and interaction with other drugs. Nondrug therapies are increasingly integrated into the treatment of dementia [7].

In the care of patients with dementia, animal-assisted therapy, especially dog assisted, is practiced more and more to improve social interaction, lessen anxiety, and reduce agitation [8]. An epidemiological study in Netherlands showed that 76% of nursing homes use animal-assisted therapy and 86% of those dogs assisted [9]. Actual studies concerning the effects of dog-assisted therapy are highly diverse in terms of design, have low case numbers, and often lack blinding as well as active control groups. Therefore, in some studies, researchers could observe a statistically significant reduction of challenging behavior by dog-assisted therapy and in another study no differences were found [8, 10, 11]. Few studies exist which examine dog-assisted therapy on inpatients in a gerontopsychiatric ward [8, 12].

Assessment of agitation in patients with severe cognitive deficits is mostly based on observation of behavior and therefore depends on the observer. In early studies focusing on animal-assisted interventions, researchers tried to assess the stress levels measuring physiological parameters like blood pressure and heart rate, which did not show significant result [13, 14]. Recently, changes in the heart rate variability (HRV) have been associated with several acute and chronic psychological stressors [15], especially the parameters corresponding with parasympathetic activity. In addition to these physiological parameters, new laboratory parameters have been recently studied in correlation with stress. For example, different types of acute and chronic stress have been associated with decreased expression of brain-derived neurotrophic factor (BDNF) [16, 17]. In the human body, BDNF mostly accumulates in megakaryocytes and circulating platelets, which have the ability to quickly release BDNF and thereby elevate its serum levels [18]. To objectify the results of our study, we decided to evaluate the effects of the therapy dog on the biological stress parameters BDNF levels and HRV. The present study aims to explore the effects of a therapy dog on the agitation of patients with dementia in a milieu therapy setting in a gerontopsychiatric ward using a blinded rater and a control group as well as biological stress parameters.

**Materials and Methods**

**Design**

The data were collected from October 2018 to September 2019 on the combined geriatric-gerontopsychiatric ward of the Oberhavel Hospital Hennigsdorf. We designed a prospective, investigator-blind intervention study, in which the patients were their own active control.

**Ethics**

This clinical trial was conducted following the Declaration of Helsinki on Ethical Principles for Medical Research. Ethical approval was obtained by the Ethics Committee Brandenburg (“Ethikkommission der Ärztekammer des Landes Brandenburg, AS99(bb)/2018). The study was registered in the German Clinical Trials Register (DRKS00024093). After an informed consent discussion over clinical trial and data processing, participants and their legal guardians gave their written consent.

**Participants**

Each patient on the gerontopsychiatric ward treated for agitation due to Alzheimer’s (late-onset) or mixed type dementia with <21 points in the Mini Mental Status Examination was asked to participate. Exclusion criteria were delirium, lack of agitation, dementia of other etiologies, allergy to dog hair, or fear of dogs. Patients were screened by the ward physicians.

**Statistics**

Using GPower 3.1, we calculated an estimated sample size of 34 patients, assuming a 2-sided t test with normal distribution, a significance level of 5%, a power of 80%, and a moderate effect size of $d = 0.5$.

**Dog and Owner**

The therapy dog named Odin is a Bernese mountain dog (weighing 50 kg) and was 4 years old at the beginning of data collection. His owner works as a physician on the ward mentioned above. Odin absolved his education to a therapy dog in the “Dog School Berlin-Brandenburg” (http://www.dogschool-bb.de/). The dog is part of the milieu therapy on the gerontopsychiatric ward. He accompanies his owner on her daily rounds, admission interviews, and family consultations. He interacts with patients for several short periods of time throughout the day.

**Parameters and Data Collection**

The clinical assessment of agitation was conducted by a rater blinded to the presence of the dog via the Overt Agitation Severity Scale (OASS [19]). The rater was a student at the University of Berlin-Brandenburg School Berlin-Brandenburg” (http://www.dogschool-bb.de/). The present study aims to explore the effects of a therapy dog on the agitation of patients with dementia in a milieu therapy setting in a gerontopsychiatric ward using a blinded rater and a control group as well as biological stress parameters.
Potsdam writing a master thesis in clinical psychology. Beforehand, she was trained for several weeks on a geriatric psychiatry ward, and she practiced the assessment of agitation of demented patients with the OASS under supervision of experienced clinical psychologists. The OASS has an observation time of 15 min. The observer rates the intensity (1–4) and frequency (0–4) of 3 items (vocalization/oral movements, upper extremities movements, and lower extremities movement). Through multiplication of intensity and frequency, a severity score is calculated for each item. The sum of all 3 severity scales is the total OASS, scoring between 0 and 48 points. The scale was performed on a day with the dog and his handler present (intervention day) and a day with only the handler present (control day) after she had ended her shift (around 16:00–18:00). Control and intervention took place within 5 days. The sequence was not randomized. Participation in the study did not change the therapy regime. Patients and the dog interacted on several occasions for a short amount of time throughout the day with an aspired total time of 20 min. Following a milieu therapy approach, the dog did not have to perform a special task, but could be petted, fed, or talked to by the patients while accompanying the resident doctor. On the control day, the contacts occurred with only the doctor present. The time of contact was recorded. There was no significant difference of the average total time spent with the patients between the 2 observation days. On-demand medication, regular medication, and coercive treatment (e.g., restraining patients against their will) were documented.

HRV was recorded via a sport watch Polar Typ V800 and matching chest strap. On both days, recording was started by the resident doctor in the morning and ended by a nurse in the evening. A corresponding 8-h interval on control and intervention day was analyzed using Kubios HRV Standard. According to the recommendations of Laborde et al. for HRV experiments, we decided to measure root mean square of successive differences (RMSSD) out of the time domain and high frequencies (HFs) out of the frequency domain to evaluate vagal tone [15].

Blood samples were taken on both days between 15:30 and 16:30. The serum tube was centrifuged over 10 min with 1,500 turns/min and stored at −70°C. The measurement was performed by a laboratory specialized in neutrophins via a highly sensitive fluorometric enzyme-linked immunoassay (ELISA) [20, 21]. To minimize the influence of unavoidable variances, BDNF levels from corresponding control probes were measured in the same assay.

Some participants denied taking a blood sample or discarded the watch or the chest strip such that difficulties occurred in the recording of the physiological stress parameters. The blood sample of 19 patients and the HRV data of 13 patients could be analyzed. An artifact rate of >5% was determined as exclusion criterion for the HRV data. Out of the 13 patients, 3 were diagnosed with atrial fibrillation, 7 took frequency modulating medication (e.g., beta-blockers), and 10 antipsychotics with cardiac side effect profile.

The statistical analysis was performed with R Studio (Version 1.3.959). As a nonparametric statistical hypothesis test for small sample size, the Wilcoxon signed-rank test to compare 2 related samples was used. We chose a significance level of $p = 0.05$.

**Results**

Out of 34 recruited patients, 8 had to be excluded from the analysis (see Fig. 1). Three patients developed delirium due to infection and were treated with antibi-
Table 1. Characteristics of the 26 patients included

| Characteristic                                | Minimum | Maximum | Median | Mean ± SD |
|-----------------------------------------------|---------|---------|--------|-----------|
| **Age, years**                                |         |         |        | 81±6      |
| **Sex, n (%)**                                |         |         |        |           |
| Female                                        | 11      |         | 42     |           |
| Male                                          | 15      |         | 58     |           |
| **Type of dementia, n (%)**                   |         |         |        |           |
| Alzheimer disease                             | 2       |         | 8      |           |
| Mixed type dementia                           | 24      |         | 92     |           |
| **MMSE, points**                              |         |         |        |           |
| Mean + SD                                     | 9.8±6.7 |         |        |           |
| Median                                        | 9.5     |         |        |           |
| Minimum                                       | 0       |         |        |           |
| Maximum                                       | 20      |         |        |           |
| **Secondary diagnosis, n**                    |         |         |        |           |
| Median                                        | 6       |         |        |           |
| IQR                                           | 2.75    |         |        |           |
| **Medications administered (substance), n**    |         |         |        |           |
| Median                                        | 8       |         |        |           |
| IQR                                           | 2.75    |         |        |           |
| **Contact time, min, mean ± SD**              |         |         |        |           |
| Intervention                                  | 22.8±7.0|         |        |           |
| Control                                       | 19.6±4.1|         |        |           |
| Control before intervention day, n (%)        | 22      |         | 85     |           |
| Intervention before control day, n (%)        | 4       |         | 15     |           |
| **On-demand medication, n (%)**               |         |         |        |           |
| Intervention day                              | 1       |         | 4      |           |
| Control day                                   | 3       |         | 12     |           |
| **Coercive treatment, n (%)**                 |         |         |        |           |
| Intervention day                              | 1       |         | 4      |           |
| Control day                                   | 0       |         | 0      |           |

Discussion

The most important study result was a reduced agitation score in patients with dementia in the presence of the therapy dog. However, a significant effect on HRV or BDNF concentrations as corresponding biological parameters could not be found.

The existing literature describes heterogeneous results concerning the effect of dog-assisted therapy on the reduction of agitation in dementia with a trend toward a positive influence. Majic et al. [22] detected no differences in the agitation of dementia patients in a nursing home measured with the Cohen-Mansfield Agitation Skala, but a significant improvement in depression. A similar case-control study of Kanamori et al. [23] showed significantly lower BEHAVE-AD scores. Both studies used an external observer scale with an observation time of 14 days but differ in location. Kanamori et al. [23] examined participants of a day care program at a psychiatric hospital, whereas Majic et al. [22] recruited habitants of a nursing home.

The longtime effect of any positive effect of dog-assisted intervention has often been questioned. A study by Richeson et al. [24] indicates that the improvement seen in the presence of the dog recedes shortly after the end of the session. In a nursing home, where a therapy dog moved in permanently, a constant improvement of agitation was observed over a 4-week period [25]. Churchill et al. [12] could also show a reduction of agitation during dog-assisted therapy in an acute care hospital.

There seems to be solid evidence of a positive effect of dog-assisted therapy on agitation symptoms in dementia patients. However, there seems to be uncertainty for the duration of this observed effect. The comparison of conducted studies is complicated due to variations in measurement tools and the length of the observation. The existing reviews criticize a lack of blinding, active controls, and randomization [8, 10–12]. Considering their repeated results, we expected a positive effect during the presence of the dog and shortly after. To avoid observation bias, we decided on an investigator-blinded design, which could only be realized by setting the observation period shortly after ending the intervention. We used a scale with a short observation time (15 min) to detect short-term effects. The interaction with the residence doctor only served as an active control. To our knowledge, the presented study is the first investigator-blinded study succeeding in showing a significant reduction of agitation in patients with dementia treated in an acute care hospital. Limitations are the small number of participants and...
the lack of randomization of the intervention/control day sequence. Comparing the time spent with the patients on control and intervention day, we see a positive tendency toward the intervention day. One explanation could be that the presence of the dog motivates patients to interact and holds their interest for a longer time. A bias of the dog handler to maximize the time patients can spend with the dog and prompt them to dwell longer should also be considered.

We aimed to evaluate parasympathetic activity via analysis of HRV as a biological stress parameter in parallel to the behavioral changes. Measurements of electrodermatological activity showed that increased agitation is correlated with a higher sympathetic and lower parasympathetic activity in patients with dementia [26]. No significant differences were found comparing mean heart rate, RMSSD, and HF with a tendency toward higher HF on the intervention day. Due to the restlessness of the participants, only 13 out of 26 measurements could be included in the analysis. The high dropout rate results in the decrease of the statistical power and therefore could explain the lack of effect on the measured parameters. Furthermore, the technical difficulties, the secondary diagnosis like atrial fibrillation, and effects of medication like beta-blockers need to be considered as confounding variables for the interpretation of the data. Van den Berg et al. [27] postulate that the HRV is mostly influenced by the vagal tone in patients with atrial fibrillation. A meta-analysis by Alvares et al. [28] concludes that neuroleptics seem to influence HRV, although at present no statement on the effect strength and the duration could be made. For beta-blocker, several studies showed an increased vagal activity [29]. In further studies, we recommend taking in consideration these confounding variables and the possible technical difficulties in undertaking HRV measurement in dementia patients.

In recent research, BDNF has been identified as a biological stress parameter but has also been researched in the context of markers for the beginning dementia [16, 30]. Low levels of BDNF correlated with the extent of cognitive deficits in patients with beginning dementia [31] and could be found postmortem in brains of Alzheimer disease patients [32]. The reduced possibilities of patients with dementia to interact with their environment could be viewed as a chronic stressor. We hypothesized that the interaction with a dog could reduce social isolation, mo-
tivate patients to interact, and so lift the BDNF level. There were no differences between control and intervention group in our study though, which could partly be due to the high dropout rate. One major confounding parameter we did not consider in our study was the quality of sleep, which has been shown to influence BDNF [33]. Deuschle et al. [34] showed that independent of a specific sleep disorder, serum BDNF levels are related to the proportion of specific sleep stages. Though we did not find differences monitoring serum BDNF levels in our setup, it would be an interesting topic of future research to evaluate long-term effects with regular therapy dog over at least 1 month.

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**Statement of Ethics**

This clinical trial was conducted following the Declaration of Helsinki on Ethical Principles for Medical Research. Ethical approval was obtained by the Ethics Committee Brandenburg (‘Ethikkommission der Ärztekammer des Landes Brandenburg, AS99(BB)/2018). The study was registered in the German Clinical Trials Register (DRKS00024093). After an informed consent discussion over clinical trial and data processing, participants and their legal guardians gave their written consent. This clinical trial was conducted following the Declaration of Helsinki on Ethical Principles for Medical Research. Ethical approval was obtained by the Ethics Committee Brandenburg (‘Ethikkommission der Ärztekammer des Landes Brandenburg, AS99(BB)/2018). The study was registered in the German Clinical Trials Register (DRKS00024093). After an informed consent discussion over clinical trial and data processing, participants and their legal guardians gave their written consent.

**Conflict of Interest Statement**

The authors report no conflicts with any product mentioned or concept discussed in this article.

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**Author Contributions**

J. Krüger, A. Ströhle, and M. Jockers-Scherübl designed the study. J. Krüger carried out the experiment. R. Izgi conducted the clinical data (OASS). R. Hellweg contributed by analyzing the BDNF levels. J. Krüger performed the statistical analysis of the data and took the lead in writing the manuscript. A. Ströhle and M. Jockers-Scherübl oversaw the research activity, planning, and execution. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

**Data Availability Statement**

The data that support the findings of this study are available from the corresponding author, Jana Krüger, upon reasonable request.

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