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ORIGINAL RESEARCH

Anthroposophic Therapy for Anxiety Disorders: A Two-year Prospective Cohort Study in Routine Outpatient Settings

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Abstract

Background and Methods: Anthroposophic treatment for anxiety disorders includes special artistic and physical therapies and special medications. We conducted a prospective cohort study of 64 consecutive adult outpatients starting anthroposophic treatment for anxiety disorders under routine conditions. Main outcomes were Anxiety Severity (physician and patient ratings 0–10), Self-rating Anxiety Scale (0–100), Center for Epidemiological Studies Depression Scale, German version (CES-D, 0–60), and SF-36 Mental Component Summary.

Results: Mean age was 42.3 years. Most frequent diagnoses were generalized anxiety disorder (44% of patients, n = 28/64) and panic disorder (39%). Median disease duration was 4.5 years. The anthroposophic treatment modalities used were medications (56% of patients), eurythmy therapy (41%), art therapy (30%), and rhythmical massage therapy (3%). Median number of eurythmy/art/massage sessions was 12, median therapy duration was 120 days.

From baseline to six-month follow-up, all outcomes improved significantly; average improvements were: Physician-rated Anxiety Severity 3.60 points (95% confidence interval 2.97–4.22, $p < 0.001$), patient-rated Anxiety Severity 3.50 (2.88–4.12, $p < 0.001$), Self-rating Anxiety Scale 11.88 (7.70–16.05, $p < 0.001$), CES-D 8.79 (5.61–11.98, $p < 0.001$), and SF-36 Mental Component 9.53 (5.98–13.08, $p < 0.001$). All improvements were maintained until last follow-up after 24 months.

Conclusions: Patients with anxiety disorders under anthroposophic treatment had long-term improvements of symptoms and quality of life.

Keywords: anthroposophy, anxiety disorders, art therapy, eurythmy therapy, prospective studies

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Background

Anxiety disorders affect 6%–19% of adults in the Western world every year[1,2] and are associated with substantial disability, reduced quality of life, reduced work capacity, and increased healthcare use.[3–8] Not all patients with anxiety disorders benefit from conventional therapy; even under the optimum conditions of a clinical trial 20%–60% of patients will not respond to psychotherapy or anti-anxiety medications.[9–13] Up to one-half of patients with anxiety symptoms use complementary therapies,[14,15] sometimes provided by their physicians.

Anthroposophic medicine (AM) is a complementary therapy system founded by Rudolf Steiner and Ita Wegman[16] and provided by specially trained physicians in 56 countries worldwide.[17] AM acknowledges a spiritual-existential dimension in man, which is assumed to interact with psychological and somatic levels in health and disease. AM therapy for anxiety disorders aims to counteract constitutional vulnerability, stimulate salutogenetic self-healing capacities, and strengthen patient autonomy.[18–20] The AM approach differs from conventional treatment in the use of special therapies (eurythmy movement exercises, art therapy, rhythmical massage therapy)[19,21] and special medications.[18]

Eurythmy therapy is an artistic exercise therapy involving cognitive, emotional and volitional elements.[22] In eurythmy therapy sessions the patients are instructed to exercise specific movements with the hands, the feet or the whole body. Eurythmy movements are related to the sounds of vowels and consonants, to music intervals or to affective gestures, e.g. sympathy-antipathy. Between therapy sessions the patients exercise eurythmy movements daily. In AM art therapy the patients engage in painting, drawing, clay modelling, music or speech exercises. Rhythmical massage therapy was developed from Swedish massage; special techniques include lifting movements, rhythmically undulating gliding movements, and complex movement patterns like lemniscates. AM medications are prepared from plants, minerals, animals and from chemically defined substances. A key concept of AM medication therapy is typological correspondences between pathophysiological processes in man and formative forces working in minerals, plants, and animals, reflecting a common evolution of man and nature.[19,23] AM therapy is provided by physicians (counselling, AM medication) and non-medical therapists (art, rhythmical massage, and eurythmy therapy). For patients with anxiety disorders the physician will choose among the available AM therapy modalities in order to tailor the treatment to individual disease features and the patient's constitution. AM treatments can be administered alone or combined with conventional psychotherapy and/or anti-anxiety medications.

To date AM therapy for anxiety disorders has been evaluated in case reports.[18,24,25] Here we present a pre-planned subgroup analysis of patients with anxiety disorders from a prospective cohort study of AM therapy.[26]

Methods

Study design and objective

This is a prospective two-year cohort study in a real-world medical setting. The study was initiated by a health insurance company as part of a research project on the effectiveness, costs, and safety of AM therapies in outpatients with chronic disease (Anthroposophic Medicine Outcomes Study, AMOS).[26] The present pre-planned analysis concerned the subgroup of adult patients with anxiety disorders. Since this was the first prospective analysis of AM therapy for this indication, the primary objective was to describe AM therapy for anxiety disorders (spectrum of anxiety indications and of AM therapy modalities used for them, extent of combination with conventional anti-anxiety therapy) as well as outcome of anxiety symptoms under AM treatment. Further research questions addressed quality of life, use of health services, adverse reactions, and therapy satisfaction.

Setting, participants, and therapy

All physicians certified by the Physicians' Association for Anthroposophical Medicine in Germany and working in an office-based practice or outpatient clinic were invited to participate in the AMOS study. Certification as an AM physician required a completed medical degree and a three-year structured postgraduate training. The participating physicians recruited consecutive patients starting AM therapy under routine clinical conditions. Patients enrolled from 1 January 1999 to 31 December 2005 were included in the present analysis if they fulfilled the eligibility criteria.

Inclusion criteria were:

1. Age 17–75 years.
2. A physician's clinical diagnosis of an anxiety disorder (International Statistical Classification of Diseases and Related Health Problems, 10th Revision [ICD-10] F40–F42 or F43.1) of at least 30 days duration.
3. Starting AM therapy for the anxiety disorder:
   3a. AM-related consultation of at least 30 minutes followed by new prescription of AM medication, or
   3b. new referral to AM therapy (art, eurythmy or rhythmical massage).

Exclusion criteria were:

1. The main indication for AM therapy is depression (only one main indication was permitted; adult AMOS patients with anxiety symptoms but with depression as main treatment indication were analysed separately).[27]
2. Previous use of the AM therapy in question (see inclusion criteria No 3) for the anxiety disorder.

The physicians' diagnostic assessment of anxiety disorders was assisted by brief written clinical descriptions of the ICD-10 diagnoses F40 Phobic anxiety disorder, F41.0 Panic disorder, F41.1 Generalized anxiety disorder (GAD), F42 Obsessive-compulsive disorder, and F43.1 Post-traumatic stress disorder. The patients were treated according to the physician's discretion. AM therapy was evaluated as a whole system.[28]

Clinical outcomes

Primary outcomes were physician- and patient-rated Anxiety Severity, assessed on numerical rating scales from 0 ("not present") to 10 ("worst possible"), at six-month follow-up. Anxiety symptoms were also assessed by the Self-Rating Anxiety Scale, German version (SAS, 0–100).[29,30] A patient self-report instrument was chosen for logistical reasons, and to avoid potential observation bias from physicians with an interest in AM having favorable outcomes. The SAS was selected among four self-report instruments available in the German language and recommended for clinical anxiety research[31] (reasons for discarding the other three instruments: Symptom-Check-List[32] because it is not specific to anxiety; Beck Anxiety Inventory[33] because it reportedly measures panic attacks rather than anxiety in general;[34] State-Trait Anxiety Inventory[30] because of the perceived lower utility of the "state" items for the present longitudinal study).

Depressive symptoms were assessed by the Center for Epidemiological Studies Depression Scale, German version (CES-D, 0–60).[35,36] Symptom Score, the severity of one to six most relevant symptoms present at baseline, was assessed by patients on numerical rating scales from 0 ("not present") to 10 ("worst possible"). Quality of life was assessed by the SF-36 Health Survey[37] (Physical and Mental Component summary measures, eight scales, Health Change item).

SAS was documented by patients enrolled after March 2001. CES-D was documented at baseline by all patients and documented during follow-up by patients enrolled after September 1999. Physician-rated Anxiety Severity was documented after 0 and 6 months, while all other clinical outcomes were documented after 0, 3, 6, 12, 18, and 24 months.

Other outcomes

Therapy outcome rating (0–10), satisfaction with therapy (0–10) and therapy effectiveness rating ("very effective, "effective", "less effective", "ineffective" or "not evaluable") were documented by the patients after 6 and 12 months.

Adverse reactions to medications or therapies were documented by the patients after 6, 12, 18 and 24 months and by the physicians after 6 months. The documentation included cause, intensity (mild /moderate/severe = no/some/complete impairment of normal daily activities), and therapy withdrawal because of adverse reactions. Serious adverse events (death, life-threatening condition, acute in-patient hospitalization, new disease or accident causing permanent disability, congenital anomaly, new malignancy) were documented by the physicians throughout the study.

Use of adjunctive therapies and health services in the pre-study year was documented at study entry, use in the first study year was documented after six and 12 months, and use in the second study year was documented after 18 and 24 months. The following items were documented: physician visits (any physician or dentist, psychiatrists), diagnostic

imaging (x-rays, computer tomography, magnetic resonance imaging, scintigrams), non-AM medications, physiotherapy, psychotherapy, inpatient hospital and rehabilitation treatment, surgery, and sick leave. Use of psychotherapy and conventional anti-anxiety medication (Anatomical Therapeutic Chemical Classification Index N05A Antipsychotics, N05B Anxiolytics, N05C Hypnotics and sedatives, N06 Antidepressants) in months 0–6 was analysed separately. Patients were classified as users if they had at least six psychotherapy sessions or used anti-anxiety medication for at least one day per month.

Data collection

All data were documented with questionnaires returned in sealed envelopes to the study office. The physicians documented eligibility criteria; the therapists documented AM therapy administration; all other items were documented by the patients, unless otherwise stated. The patient responses were not made available to the physicians. The physicians were compensated 40 Euro (after March 2001: 60 Euro) per included and fully documented patient, while the patients received no compensation.

The data were entered twice by two different persons into Microsoft® Access 97. The two datasets were compared and discrepancies resolved by checking with the original data.

Quality assurance, adherence to regulations

The study was approved by the Ethics Committee of the Faculty of Medicine Charité, Humboldt University Berlin, and was conducted according to the Helsinki Declaration and largely following the ICH Guideline for Good Clinical Practice E6. Written informed consent was obtained from all patients before enrolment.

Data analysis

The data analysis was performed on all patients fulfilling the eligibility criteria, using SPSS® 14.0.1 (SPSS Inc., Chicago, Ill, USA) and StatXact® 5.0.3 (Cytel Software Corporation, Cambridge, MA, USA). T-test was used for continuous data with normal distribution; Wilcoxon Signed-Rank test was used for paired continuous data with non-normal distribution; McNemar test and Fisher's exact test were used for dichotomous data. All tests were two-tailed. Significance criterion was $p < 0.05$. Since this was a descriptive study, no adjustment for multiple comparisons was performed.[38] Pre-post effect sizes were calculated as Standardised Response Mean (= mean change score divided by the standard deviation of the change score) and classified as minimal (<0.20), small (0.20–0.49), medium (0.50–0.79), and large (≥0.80).[39,40] In the main analysis, clinical outcomes were analysed in patients with evaluable data for each follow-up, without replacement of missing values.

Three pre-planned sensitivity analyses (SA1–SA3) were performed to assess the influence of patient attrition, natural recovery, and conventional anti-anxiety therapies on the 0–6-month outcome of physician- and patient-rated Anxiety Severity. SA1 concerned attrition bias: Missing values after six months were replaced with the last value carried forward. SA2 concerned natural recovery, which was assumed to be unlikely in patients with disease duration of at least one year:[41] The sample was restricted to patients with disease duration of at least 12 months prior to study enrolment. SA3 concerned the effects of conventional anti-anxiety therapies (see Other Outcomes, above, for details). The sample was restricted to patients not using conventional anti-anxiety therapies during the first six study months. Post-hoc subgroup analyses were performed on evaluable diagnostic groups and AM therapy modality groups.

Results

Participating physicians and therapists

The patients were enrolled by 29 physicians with four different qualifications (22 general practitioners, three psychiatrists, two internists, and two gynaecologists). Comparing these physicians to AM-certified physicians in Germany with the same four qualifications but without study patients (n = 237), no significant differences were found regarding gender (48.3% vs. 60.3% males), age (48.5 ± 7.7 vs. 47.9 ± 7.9), number of years in practice (19.9 ± 8.1 vs. 19.2 ± 9.1), and the proportion of physicians working in primary care (82.8% vs. 86.2%).

The patients were treated by 36 different AM therapists (eurythmy, art, rhythmical massage). Comparing these therapists to certified therapists

without study patients (n = 1131), no significant differences were found regarding gender (86.1% vs. 80.8% women), age (mean 50.1 ± 9.6 vs. 50.2 ± 9.4 years) or the number of years since therapist qualification (11.7 ± 7.4 vs. 13.1 ± 8.7 years).

Patient recruitment and follow-up

A total of 75 patients starting AM therapies for anxiety disorders were screened for inclusion. Of these patients, 64 fulfilled all eligibility criteria and were included in the analysis. Eleven patients were not included; in two of these patients the eligibility criteria were not fulfilled (previous study participation: n = 1; ongoing use of AM therapy in question: n = 1). The remaining nine patients were potentially eligible but not included for the following reasons: no informed consent (n = 4), physician's baseline documentation incomplete (n = 3), patients' and physicians' baseline questionnaire dated >30 days apart (n = 1), administrative reasons (n = 1). Included patients (n = 64) and potentially eligible but not included patients (n = 9) did not differ significantly regarding age, gender, duration of anxiety disorder or evaluable baseline scores (physician and patient-rated Anxiety Severity, Symptom Score).

A total of 78% of patients (n = 50/64) were enrolled by general practitioners, 13% (n = 8) by psychiatrists, 6% (n = 4) by internists, and 3% (n = 2) by gynaecologists. The physicians' settings were primary care practices (84% of patients, n = 54/64), referral practice (14%, n = 9), and outpatient clinics (2%, n = 1). Each physician enrolled 1–2 patients (69%, n = 20/29 physicians), 3–4 patients (21%, n = 6), or 5–6 patients (10%, n = 3).

The last patient follow-up ensued on 21 November 2007. A total of 94% (60/64) of patients returned at least one follow-up questionnaire. The patients were administered a total of 320 follow-up questionnaires, out of which 252 (79%) were returned. Follow-up rates were 88% (n = 56/64), 80%, 78%, 77%, and 80% after 3, 6, 12, 18, and 24 months, respectively. Respondents (n = 50) and non-respondents (n = 14) of the six-month follow-up questionnaire did not differ significantly regarding age, gender, disease duration or baseline parameters (physician- and patient-rated Anxiety Severity, SAS, Symptom Score). Corresponding dropout analysis for the 24-month follow also showed no significant differences between respondents (n = 51) and non-respondents (n = 13). The physician six-month follow-up documentation was available for 94% (60/64) of patients.

Baseline characteristics

The patients were recruited from 9 of 16 German federal states. Age groups were 19–29 years (16%, n = 10/64), 30–49 years (58%, n = 37), and 50–69 years (27%, n = 17) with a mean age of 42.3 ± 11.4 years (range 19–68 years). A total of 86% (n = 55/64) of the patients were women. Compared with the German population, patients had higher educational and occupational levels and were less frequently regular smokers, daily alcohol consumers, and overweight. Socio-demographic status was similar to the population regarding unemployment, severe disability status, sports activities, and the proportion of patients living alone and less favourable for work disability pension and sick-leave (Table 1).

A total of 36% (n = 23/64) of patients had more than one anxiety diagnosis, while 55% (n = 35/64) had more than one mental diagnosis (ICD-10 F00–F99). Most frequent anxiety diagnoses were GAD (44% of patients) and panic disorder (39%) (Table 2). Median duration of the anxiety disorder was 4.5 years (interquartile range [IQR] 1.0–20.0 years, range 6 weeks to 40 years, mean 9.5 ± 10.4 years).

A current comorbid non-anxiety disease was present in 81% (52/64) of patients, with a median of 2 (IQR 1–3) comorbid diseases per patient. Most common comorbid diseases, classified by ICD-10, were musculoskeletal, gastrointestinal and circulatory diseases (Table 2). Most common comorbid non-anxiety mental disorders (ICD-10 three-digit codes) were F32 Depressive episode (8% of patients, n = 5/64) and F48 Other neurotic disorder (3%, n = 2). A total of 74% (45/61) of evaluable patients had clinically relevant depressive symptoms (CES-D ≥ 24 points.[42]) In the pre-study year the patients had had an average of 7.1 ± 12.2 visits to psychiatrists (0 visits: n = 27/61 evaluable patients; 1–7 visits: n = 15/61; ≥8 visits: n = 19/61) and 7.8 ± 14.2 psychotherapy sessions (0 sessions: n = 35/63 evaluable patients, 1–7 sessions: n = 6/63, ≥8 sessions: n = 22/63).

Table 1. Socio-demographic data.

Item	Subgroup	Study patients		German adult population	Source
		N	%	%	
Education[53]	Low (level 1)	17/64	27%	43%	[54]
	Intermediate (level 2)	38/64	59%	43%	
	High (level 3)	9/64	14%	14%	
Wage earners		4/41	10%	18%	[55]
Unemployed during last 12 months	Economically active patients	4/41	10%	10%	[55]
Living alone		14/64	22%	21%	[55]
Net family income < 900 € per month		14/50	28%	16%	[55]
Alcohol use daily (patients) vs. almost daily (Germany)	Male	1/9	11%	28%	[56]
	Female	1/55	2%	11%	
Regular smoking	Male	1/9	11%	37%	[57]
	Female	6/55	11%	28%	
Sports activity ≥1 hour weekly	Age 25–69	25/57	44%	39%	[58]
Body mass index ≥25 (overweight)	Male	2/8	22%	56%	[55]
	Female	14/55	26%	39%	
Permanent work disability pension		5/64	8%	3%	[59]
Severe disability status		6/64	9%	12%	[60]
Sick leave days in the last 12 months (mean ± SD)	Economically active patients	45,5 ± 84,47		17.0%	[61]

Therapy

At study enrolment, the duration of the consultation with the AM physician was <30 min in 53% (n = 34/64) of patients, 30–44 min in 23% (n = 15), 45–59 min in 5% (n = 3), and ≥60 min in 19% (n = 12). At enrolment 9% (n = 6/64) of patients fulfilled Inclusion Criterion 3a (AM-related consultation of ≥30 minutes followed by new prescription of AM medication), 80% (n = 51) fulfilled Inclusion Criterion 3b (referrall to AM eurythmy/art/massage therapy), and 11% (n = 7) fulfilled Inclusion Criteria 3a and 3b. Of the 58 patients referred to AM eurythmy/art/massage therapy, 81% (n = 47) had the planned AM therapy, 3% (n = 2) did not have AM therapy, and for 16% (n = 9) the AM therapy documentation is incomplete. AM therapies used were eurythmy therapy (n = 26 patients), rhythmical massage therapy (n = 2), and art therapy (n = 19) with the therapy modalities painting/drawing/clay (n = 13), speech exercises (n = 4), and music (n = 2). The AM therapy started median 5 (IQR 0–36) days after enrolment. Median therapy duration was 120 days (IQR 92–175 days, mean 153.2 ± 96.7 days), median number of therapy sessions was 12 (IQR 10–19, mean 15.1 ± 8.2 sessions). During the 24-month follow-up, 56% (n = 36/64) of patients used AM medications for anxiety or other indications.

The use of adjunctive therapies, health services, and sick leave was compared between the pre-study year and the first and second years, respectively. Two significant changes were found: The number of psychotherapy sessions increased from average 7.8 ± 14.3 sessions in the pre-study year to 12.1 ± 17.5 sessions in the first year (p = 0.026), and the number of inpatient rehabilitation days decreased from 3.8 ± 12.4 days in the pre-study year to 0.0 ± 0.0 days in the second year (p = 0.024). The number of evaluable patients receiving inpatient rehabilitation was n = 8/64 in the pre-study year, n = 1/49 in the first

Table 2. Disease status at baseline.

ICD-10	Diagnosis of anxiety disorder (n = 64 patients, multiple responses possible)	N	%
F41.1	Generalized anxiety disorder	28	44%
F41.0	Panic disorder	25	39%
F40	Phobic anxiety disorder	15	23%
F42	Obsessive-compulsive disorder	7	11%
F43.1	Post-traumatic stress disorder	5	8%
F41.9	Anxiety disorder, unspecified	4	6%
F41.8	Other specified anxiety disorders	3	5%
	Duration of anxiety disorder (n = 64 patients)		
	1–5 months	4	6%
	6–11 months	7	11%
	1–4 years	21	33%
	≥5 years	32	50%
ICD-10	**Non-anxiety comorbid diseases (n = 122 diagnoses)**		
M00-M99	Diseases of the musculoskeletal system and connective tissue	25	20%
K00-K93	Diseases of the digestive system	17	14%
I00-I99	Diseases of the circulatory system	15	12%
F00-F99	Mental and behavioural disorders	13	11%
E00-E90	Endocrine, nutritional and metabolic diseases	11	9%
	Other diagnoses	41	34%

ICD-10: International statistical classification of diseases and related health problems, 10th revision.

study year, and n = 0/46 in the second year. No other items (number of physician/dentist or psychiatrist visits, diagnostic imaging, non-AM medications, physiotherapy, inpatient hospitalisation, surgery, sick leave) changed significantly in any period.

The use of psychotherapy and conventional anti-anxiety medications in months 0–6 was analysed separately. A total of 33% (n = 17/51) of evaluable patients had psychotherapy, 24% (n = 12/51) used conventional anti-anxiety medications (see Methods for definition), while 55% (n = 28/51) used neither psychotherapy nor anti-anxiety medications.

Clinical outcomes

All clinical outcomes were improved from baseline at all subsequent follow-ups (Figs. 1–5). For 12 of the 16 outcomes (physician- and patient-rated Anxiety Severity, SAS, CES-D, Symptom Score, and seven SF-36 scores) all improvements from baseline were significant at all follow-ups. The SF-36 scales Physical Function and Role Physical did not improve significantly in months 0–3, but at subsequent follow-ups all improvements from baseline were significant (except Physical Function in months 0–24). SF-36 Physical Component summary and the SF-36 scale Bodily Pain did not improve significantly at any follow-ups (except Bodily Pain in months 0–12).

At six-month follow-up an improvement of ≥50% of baseline Anxiety Severity was observed in 57% (n = 25/44) of evaluable patients for patient rating and in 58% (n = 33/57) for physician rating. Effect sizes for the 0–6-month comparison were large for nine outcomes (physician- and patient-rated Anxiety Severity, Symptom Score, SAS, CES-D, and four SF-36 scores), medium for one outcome, and small for six outcomes (Table 2). Subgroup analyses showed similar improvement in evaluable diagnostic groups (GAD, panic disorder) and therapy modality groups (eurythmy therapy, AM art therapy) (Table 3).

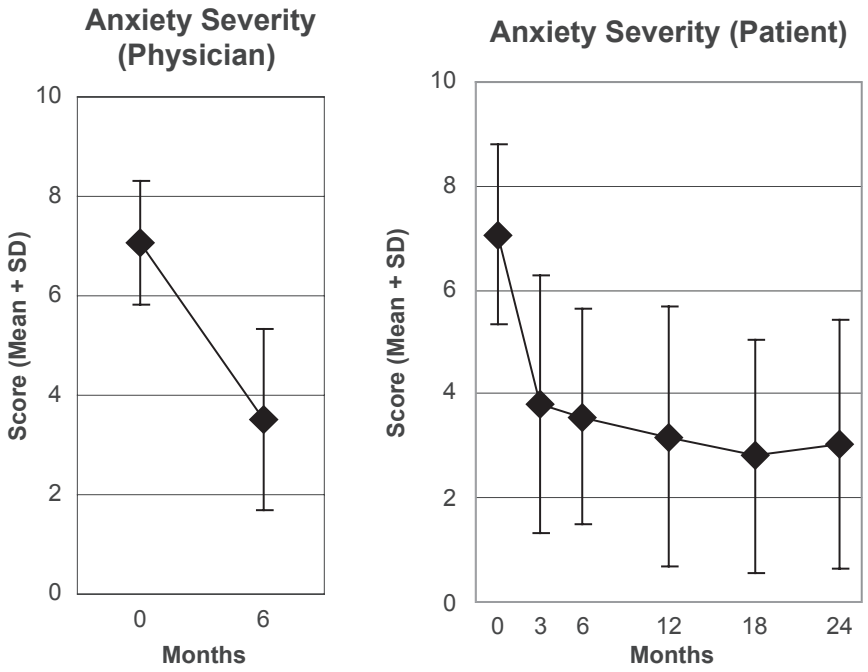

Figure 1. Anxiety Severity. Range: 0 "not present", 10 "worst possible". Physician rating, n = 63. Patient rating, n = 56.

We performed three sensitivity analyses of the 0–6-month outcome of physician- and patient-rated Anxiety Severity (Table 4: SA1–SA3; see Methods for further description). For physician rating, the individual analyses resulted in a reduction of the average 0–6 month improvement of maximum 11% (3.60→3.22 points). Combining all three analyses, the improvement was reduced by 12%

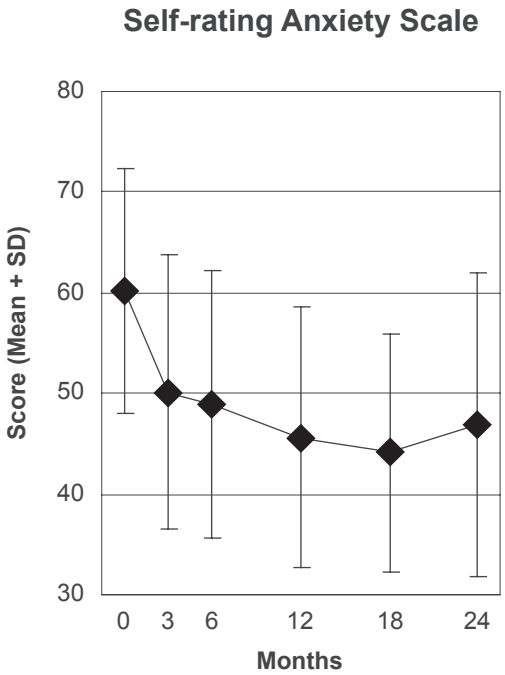

Figure 2. Self-rating Anxiety Scale. Range 0–100, higher scores indicate more anxiety symptoms. Patients enrolled after March 2001, n = 38.

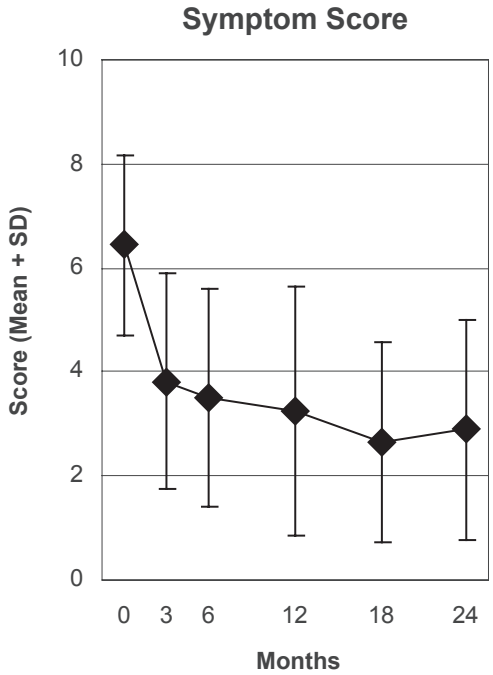

Figure 3. Symptom Score. Range: 0 "not present", 10 "worst possible". Patient rating, n = 63.

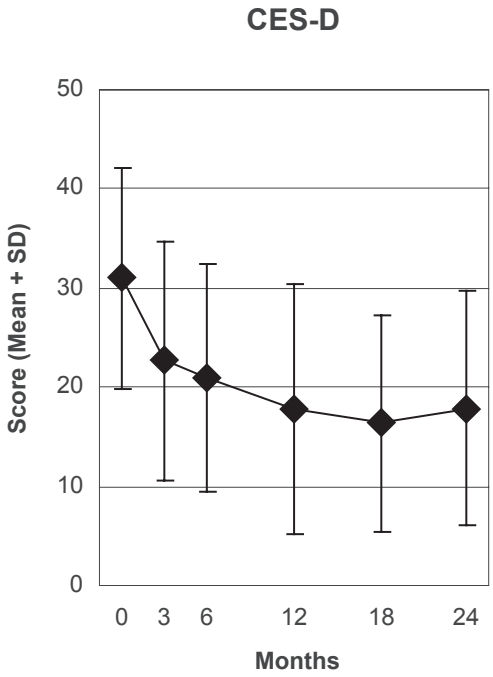

Figure 4. Center for Epidemiological Studies Depression Scale, German version (CES-D). Range: 0–60, higher scores indicate more depressive symptoms. Patients enrolled after September 1999, n = 55.

(3.60→3.17 points). For patient rating, the individual analyses resulted in a reduction of the improvement of maximum 14% (3.50→3.00 points). Combining all three analyses, the improvement was increased by 3% (3.50→3.59 points).

Other outcomes

At six-month follow-up, patients' average therapy outcome rating (numeric scale from 0 "no help at all" to 10 "helped very well") was 6.82 ± 2.74 and patient satisfaction with therapy (from 0 "very dissatisfied" to 10 "very satisfied") was 7.61 ± 2.65. The patients' effectiveness rating of eurythmy, art or rhythmical massage therapy was positive ("very effective" or "effective") in 86% (37/43) of evaluable patients who had started therapy, and negative ("less effective", "ineffective" or "not evaluable") in 14%. The ratings of therapy outcome, satisfaction, and effectiveness did not change significantly between 6- and 12-month follow-up.

The frequency of reported adverse drug reactions was 14% (n = 5 of 36 users) for AM medications and 14% (n = 7 of 50 users) for non-AM medications. Adverse drug reactions of severe intensity were reported in six patients (AM medications: n = 3, non-AM medications: n = 3), while medication was stopped due to reported adverse reactions in eight patients (AM medications: n = 5, non-AM medications: n = 3). Adverse reactions from non-medication therapies were reported in four patients (eurythmy therapy: n = 2, psychotherapy: n = 1, Dorn therapy: n = 1). Two serious adverse events occurred: One patient was acutely hospitalized for 34 days for panic disorder, and one patient died from Acquired Immunodeficiency Syndrome (AIDS). None of these events were related to any therapy or medication.

Discussion

This is the first prospective evaluation of AM treatment for anxiety disorders. We aimed to obtain information on AM therapy for this indication under routine outpatient conditions in Germany and studied adults starting AM therapy for anxiety disorders. Most frequent anxiety diagnoses were GAD, panic disorder, and phobic disorders. Two-third of patients engaged in eurythmy movement exercises or artistic therapies; half of patients used AM medications; one-fourth used conventional anti-anxiety medications. Under AM treatment, significant and sustained improvements of anxiety symptoms, other symptoms, and quality of life were observed.

Strengths of this study include a detailed assessment of the therapy setting and therapy-related factors, a long follow-up period, and a high representativeness: 11% of all AM-certified physicians seeing anxiety patients in Germany participated, the participating AM physicians and therapists resembled all eligible physicians and therapists with respect to socio-demographic characteristics, and 88% of screened and eligible patients were enrolled. These features suggest that the study to a high degree mirrors contemporary AM practice.

Because the frequency of individual anxiety diagnoses in AM outpatient care was largely unknown prior to the study, we included patients with a range of anxiety diagnoses. Also, to mirror clinical practice, where the selection of AM therapy options will vary according to individual features, we assessed AM as a whole system.[28] Supplementary subgroup analyses were possible and showed similar improvements in patients with GAD and panic disorder, and in patients receiving eurythmy therapy and AM art therapy. However, the sample size for other anxiety diagnoses

Table 3. Clinical outcomes (0–6 months).

Outcome (range)	N	0 months	6 months	0–6 month difference*		SRM	Score values in adult population
		Mean (SD)	Mean (SD)	Mean (95%-CI)	P-value		Mean (SD)
Anxiety Severity, Physician (0–10)							No data
• All diagnoses and therapies	57	7.16 (1.18)	3.56 (1.80)	3.60 (2.97 to 4.22)	<0.001	1.52	
• Generalized anxiety disorder	23	6.96 (1.22)	3.43 (1.38)	3.52 (2.70 to 4.35)	<0.001	1.85	
• Panic disorder	22	7.27 (1.12)	3.18 (1.76)	4.09 (3.06 to 5.12)	<0.001	1.76	
• Eurythmy therapy	32	7.09 (1.17)	3.44 (1.81)	3.66 (2.78 to 4.53)	<0.001	1.51	
• AM art therapy	16	7.06 (1.39)	3.75 (1.95)	3.31 (1.90 to 4.73)	<0.001	1.25	
Anxiety Severity, Patient (0–10)							No data
• All diagnoses and therapies	44	7.09 (1.72)	3.59 (2.08)	3.50 (2.88 to 4.12)	<0.001	1.71	
• Generalized anxiety disorder	19	7.42 (1.26)	3.63 (1.83)	3.79 (2.98 to 4.60)	<0.001	2.25	
• Panic disorder	17	7.06 (1.52)	3.29 (1.83)	3.76 (2.79 to 4.74)	<0.001	1.99	
• Eurythmy therapy	24	6.75 (1.82)	3.42 (1.79)	3.33 (2.43 to 4.24)	<0.001	1.56	
• AM art therapy	14	7.64 (1.34)	3.93 (2.64)	3.71 (2.40 to 5.02)	<0.001	1.64	
Symptom Score (0–10)	49	6.35 (1.70)	3.52 (2.09)	2.83 (2.30 to 3.37)	<0.001	1.52	No data
SAS (0–100)	26	60.91 (13.12)	49.04 (13.52)	11.88 (7.70 to 16.05)	<0.001	1.15	27.0 (4.7)[30]
CES-D (0–60)	41	31.04 (11.87)	22.24 (11.94)	8.79 (5.61 to 11.98)	<0.001	0.87	14.33 (9.66)[36]
SF-36 Physical Component	50	47.64 (10.87)	49.01 (9.86)	1.36 (–1.29 to 4.02)	0.306	0.15	50.44 (10.08)[62]
SF-36 Mental Component	50	28.71 (10.31)	38.24 (11.37)	9.53 (5.98 to 13.08)	<0.001	0.76	50.84 (8.70)[62]
SF-36 Scales (0–100)							
• Physical Function	50	76.88 (25.24)	83.92 (21.15)	7.04 (1.54 to 12.55)	0.013	0.36	87.09 (20.65)[62]
• Role Physical	50	51.50 (39.58)	65.00 (40.72)	13.50 (0.97 to 26.03)	0.035	0.31	82.94 (32.58)[62]
• Role Emotional	50	34.00 (37.19)	56.00 (42.29)	22.00 (8.12 to 35.88)	0.003	0.45	88.49 (27.80)[62]
• Social Functioning	50	47.00 (26.07)	65.50 (26.19)	18.50 (12.36 to 24.64)	<0.001	0.86	88.27 (18.90)[62]
• Mental Health	50	36.96 (17.31)	53.20 (17.84)	16.24 (11.24 to 21.24)	<0.001	0.92	73.15 (17.28)[62]
• Bodily Pain	50	60.84 (31.42)	68.52 (28.64)	7.68 (–0.87 to 16.23)	0.077	0.26	78.85 (27.79)[62]
• Vitality	50	33.50 (18.41)	47.70 (19.95)	14.20 (9.18 to 19.22)	<0.001	0.80	62.89 (18.36)[62]
• General Health	50	47.84 (18.86)	53.98 (22.42)	6.14 (0.92 to 11.36)	0.022	0.33	67.46 (20.33)[62]
SF-36 Health Change**	50	3.42 (1.14)	2.24 (1.08)	1.18 (0.80 to 1.56)	<0.001	0.89	2.92 (0.99)[62]

SAS: Self-rating Anxiety Scale, documented in patient enrolled after March 2001. CES-D: Center for Epidemiological Studies Depression Scale, German version. *Positive differences indicate improvement. **SF-36 Health Change: range from 1 ("much better now than one year ago") to 5 ("much worse now than one year ago"). SRM: Standardised Response Mean effect size (minimal: <0.20, small: 0.20–0.49, medium: 0.50–0.79, large: ≥0.80)

Table 4. Anxiety Severity 0–6 months: sensitivity analyses.

Outcome/Analysis	N	0 months	6 months	0–6 month difference	
		Mean (SD)	Mean (SD)	Mean (95%-CI)	P-value
Physician rating					
Main analysis: Patients with evaluable data at 0 and 6 months	57	7.16 (1.18)	3.56 (1.80)	3.60 (2.97–4.22)	<0.001
SA1: Last value carried forward	63	7.06 (1.26)	3.81(1.94)	3.25 (2.63–3.88)	<0.001
SA2: Patients with a disease duration of ≥12 months	50	6.98 (1.19)	3.74 (1.80)	3.22 (2.57–3.88)	<0.001
SA3: Patients not using conventional anti-anxiety therapy in months 0–6	27	7.07 (1.38)	3.48 (1.65)	3.59 (2.71–4.48)	<0.001
SA1 + SA2 + SA3	23	6.83 (1.34)	3.65 (1.70)	3.17 (2.26–4.08)	<0.001
Patient rating					
Main analysis: Patients with evaluable data at 0 and 6 months	44	7.09 (1.72)	3.59 (2.08)	3.50 (2.88–4.12)	<0.001
SA1: Last value carried forward	61	7.08 (1.82)	4.08 (2.47)	3.00 (2.42–3.58)	<0.001
SA2: Patients with a disease duration of ≥12 months	39	7.23 (1.84)	3.77 (2.25)	3.46 (2.82–4.10)	<0.001
SA3: Patients not using conventional anti-anxiety therapy in months 0–6	27	6.89 (1.85)	3.21 (1.97)	3.63 (2.84–4.42)	<0.001
SA1 + SA2 + SA3	22	7.09 (1.80)	3.50 (2.11)	3.59 (2.73–4.45)	<0.001

and other AM therapy modality subgroups (medical, rhythmical massage) did not allow for subgroup analysis. Diagnosis, therapy modality, and other predictors of clinical outcome will also be addressed in a multivariate analysis of a larger dataset from the AMOS study (submitted for publication).

To accommodate the study documentation to any anxiety disorder, clinical outcomes did not include a diagnosis-specific instrument for panic disorder,[31] while the SAS, a recommended instrument for GAD,[31] was only documented in a subset of patients.

Since the study had a long recruitment period, the study physicians were not able to participate throughout the period and to screen and enrol all eligible patients (criteria: see Methods section). For a different subset of patients from the AMOS project (patients referred to AM therapies for any chronic indication and enrolled before 1 April 2001), it was estimated that physicians enrolled every fourth eligible patient.[27] This selection could bias results if physicians were able to predict therapy response and if they preferentially screened and enrolled such patients for whom they expected a particularly favourable outcome. In this case one would expect the degree of selection (= the proportion of eligible vs. enrolled patients) to correlate positively with clinical outcomes. That was not the case, the correlation was almost zero (–0.04). This analysis[27] does not suggest that physicians' screening of eligible patients was affected by selection bias.

A limitation of the study is the absence of a comparison group receiving conventional treatment or no therapy. Accordingly, for the observed improvements one has to consider several other causes apart from the AM treatment. We therefore conducted a sensitivity analysis of physician- and patient-rated Anxiety Severity, estimating the influence of attrition bias, natural recovery, and adjunctive therapies. These three factors together explained up till 12% of the 0–6 month improvement. According to a previous analysis from this research program,[41] regression to the mean due to symptom fluctuation with preferential self-selection to therapy and study inclusion at symptom peaks explained up till 0.43 points (12%) of the improvement of an outcome corresponding to physician-rated Anxiety Severity in this analysis.

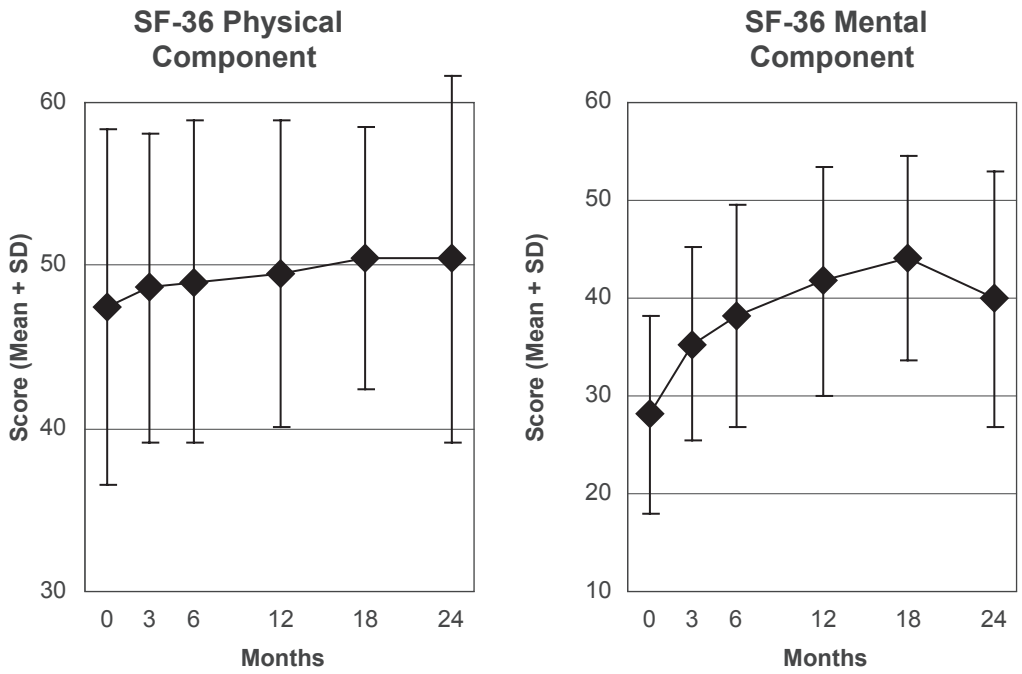

Figure 5. SF-36 Physical and Mental Component summary measures. Higher scores indicate better health, n = 63.

Other possible confounders are psychological factors and non-specific effects. However, since AM therapy was evaluated as a whole system,[28] the question of specific therapy effects vs. non-specific effects (placebo effects, context effects, physician-patient interactions, patient expectations etc.) was not an issue of the present analysis.

Because 16 clinical outcomes were analysed with a total of 20 comparisons at six-month follow-up (Table 2), the issue of multiple hypothesis-testing arises.[38] However, 18 of the 20 comparisons showed significant improvements and 14 comparisons had p-values < 0.001.

This study provides the first data on the treatment of anxiety disorders in AM settings. The female/male ratio in this predominantly primary care sample (6.1/1.0) was higher than in German primary care patients with GAD (2.1/1.0)[43] or in German population samples with GAD (2.1/1.0)[44] or any anxiety disorder (2.2/1.0).[45] The higher proportion of women in this sample is in accordance with other studies of AM patients with chronic disease.[19,46,47] This finding might possibly reflect that women are more likely than men to engage in creative therapies such as AM art therapy and eurythmy therapy. Most frequent diagnoses were GAD, panic disorders, and phobic disorders, which is in accordance with data from German primary care.[48] The proportion of patients with more than one mental diagnosis (55%) was similar to the proportion among adults with anxiety disorders in the German population (62%).[45] However, these diagnostic comparisons should be treated with caution, since the diagnosis of mental disorders in our study was based on physicians' clinical diagnosis and not on a criteria-based assessment, apart from brief clinical descriptors of anxiety diagnoses. This feature may have lead to an underestimation of comorbid mental diagnoses in our study, as suggested by the low frequency of a physician's diagnosis of depression (8% of patients) compared to the high proportion of patients with clinically relevant depressive symptoms (74%).

Baseline anxiety symptom severity, assessed by the SAS, was one-half to one standard deviation higher than baseline scores in clinical trials of anxiety patients from German primary care.[49,50] Mental quality of life at baseline, assessed with the SF-36 Mental Component summary (28 points in all patients, 29 points in patients with GAD), was one-third standard deviation worse than in German adults with GAD.[44] Other anxiety-related baseline data such as number of anxiety episodes, recent crises or psychiatric inpatient hospitalizations were

not documented and can therefore not be compared to other studies. The proportion of responders at six-month follow-up (patients with 50% improvement of Anxiety Severity from baseline: 57%–58%) was of the same order of magnitude as responder rates in trials of anti-anxiety medications or psychotherapy.[9,10,13]

Previous studies have found beneficial effects of AM therapies on anxiety in cancer patients.[51,52] The present study is the first to demonstrate improvement of patients with anxiety disorders under AM treatment.

In the first six months after enrolment, 55% of study patients had no standard therapy (psychotherapy, anti-anxiety medication). Some patients with anxiety disorders will not profit from standard therapies; other patients discontinue standard therapies due to adverse reactions or reject them because they are passive (medication) or can be felt as intrusive or too verbal (psychotherapy). In this context, the AM non-verbal and artistic exercising therapies offer a different approach or even a bridge to opening up communication on a verbal level.[19]

Conclusions

In this study, adults with anxiety disorders under AM treatment had long-term reduction of symptoms and improvement of quality of life. Improvements were similar in patients not using anti-anxiety medications or psychotherapy. Although the pre-post design of the present study does not allow for conclusions about comparative effectiveness, study findings suggest that AM therapies may be useful in the long-term care of patients with anxiety disorders.

List of Abbreviations

±, standard deviation; AM, Anthroposophic Medicine; AMOS, Anthroposophic Medicine Outcomes Study; CES-D, Center for Epidemiological Studies Depression Scale, German version; GAD, Generalized anxiety disorder; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision; IQR, interquartile range; SA, Sensitivity analysis; SAS, Self-Rating Anxiety Scale.

Competing Interests

Within the last five years HJH and GSK have received restricted research grants from the pharmaceutical companies Weleda and Wala, who produce AM medications. Otherwise all authors declare that they have no competing interests.

Authors' Contributions

HJH, CMW, GSK, SNW, and HK contributed to study design. HJH, AG, and HK contributed to data collection. HJH, RZ, and HK wrote the analysis plan, HJH and AG analysed data. HJH was principal author of the paper, had full access to all data, and is guarantor. All authors contributed to manuscript drafting and revision and approved the final manuscript.

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