INTRODUCTION

Multiple sclerosis (MS) is a neuroinflammatory and neurodegenerative disease affecting mostly young adults between 20-40 years of age. Women are about two to three times more often affected than men.\textsuperscript{1,2} Despite emerging treatments in MS (both immune-modulatory as well as symptomatic ones), causal and symptom-focused MS therapies are not available at cure resorts. The physical limitations and psychological impacts resulting from MS require adaptations of life plans.\textsuperscript{3} Because of its unpredictable course, MS
represents a great challenge to patients. They have to cope with the disease and associated changes in life. These continuously functional and psychosocial changes may result in psychological problems such as depression or impairment of social cognition,\textsuperscript{4,5} which are seen more frequently in patients with advanced disability.\textsuperscript{3,4} The prevalence of depression is between 30% and 50% in MS patients over course of disease.\textsuperscript{4,6} As a consequence, the suicide rate in MS patients is recognizable higher than in the general population.\textsuperscript{7} MS causes multiple stressors, which all require different methods of coping. They seem to be influenced by the level of impairment. Especially, moderate affected patients are tackling more intensively with their disease in comparison with less or more severe impaired patients.\textsuperscript{8} One way of coping is to look for other and/or additional forms of treatment: the so-called complementary and alternative medicine (CAM).\textsuperscript{9} CAM is defined as a group of medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.\textsuperscript{8,10,11} Therapies are either used together with (complementary therapies) or in place of conventional therapies (alternative therapies). There is insufficient knowledge about the connection between the coping behavior and CAM utilization in MS patients. From research in oncology, it is known that CAM users tend to deal more actively with the disease and use coping strategies with focus on perceived problems.\textsuperscript{12} Similar results have been reported in MS.\textsuperscript{3,11,13} However, nonusers reported better compliance and higher confidence in their physician. Early studies suggested that CAM utilization was an indicator for psychosocial difficulties in MS patients.\textsuperscript{14} Altogether, there is insufficient knowledge about the motives of patients using CAM, as well as the connection between the coping behavior of MS patients and CAM utilization.

The aim of the study is to investigate the differences in coping behavior between CAM users and nonusers, and additional influencing factors.

2 | MATERIAL AND METHODS

Socio-demographic variables and MS-specific characteristics were collected in a semistructured interview. Aspects of coping and the level of depression were investigated by means of standardized self-assessment instruments, namely the Trier Illness Coping Scales and the Beck Depression Inventory. In order to be included in the study, patients had to be diagnosed with definite MS (following the revised McDonalds criteria in its respective applicable version\textsuperscript{15,16}). Patients took voluntarily part in the study by informed consent. The information gathered throughout the interview was completed by data derived from neurological examinations (e.g., course of illness and Expanded Disability Status Scale (EDSS) score), carried out by experienced neurologists of the participating clinics. The study was approved by the local ethics committee (A2011-0125).

2.1 | Trier illness coping scales

The coping behavior of the MS patients was assessed with the Trier Illness Coping Scales (TSK) from Klauer and Filipp.\textsuperscript{17} The standardized questionnaire includes thirty-seven items with a six-grade scale, which are combined to five subscales, and characteristics of cognitive and behavioral strategies of coping are assessed. The TSK is evaluated for over 900 patients with different diseases including cancer, MS, rheumatoid spondylitis, HIV, and chronic renal insufficiency.\textsuperscript{8,17} The five subscales can be described as follows:

1. Rumination specifies brooding thoughts about previous illness-related problems. Patients with high scores on this scale are searching for causes of their illness in the past and draw comparisons to the time before disease onset.
2. Defense of threat is an intra-psyismic coping style that combines palliative cognitive reactions like revaluation and downward comparison.
3. Search for social integration describes turning toward social environment to mobilize emotional support and to distract from illness-related problems.
4. Search for information and exchange of experience characterizes an active coping style, where patients are looking for social support and information about the disease and treatment options in an active manner.
5. Search for support in religion is a scale which reflects the personal preferences for religion as a coping resource.

2.2 | Beck depression inventory

The Beck Depression Inventory (BDI) was used for assessing the occurrence of acute symptoms of depression.\textsuperscript{18} When adding the single items to a total value, The items “work difficulties,” “fatigue” and “concerns about health” were excluded from evaluation due to being possible confounders with MS-related symptoms.\textsuperscript{19}

2.2.1 | Sample description

A total of 254 patients with definite MS were included in this cross-sectional study. All patients were recruited at the Department of Neurology and Outpatient Services at the University of Rostock (n = 154) and at the Marianne-Strauss-Clinic in Berg/Kempfenhausen (n = 100). Patients visited both institutions either for routine check-up or because of acute disease exacerbation. All eligible patients agreed to participate in the study.

About 73.6% of the examined MS patients were women, which approximates the general MS population. Patients were on average 44.0 years old (SD=11.6) and MS was diagnosed on average 8.1 years (SD=7.0) prior to the interview. The median EDSS was 4.0 (SD=2.2). Most of the patients (56.3%) suffered from relapsing-remitting MS
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**TABLE 1**  Basic characteristics of enrolled patients

| Sex    | RRMS | SPMS | PPMS | EDSS (median) | Disease duration (years) |
|--------|------|------|------|---------------|--------------------------|
| Male   | 30   | 32   | 5    | 4.6 (5.0)    | 8.0                      |
| Female | 113  | 64   | 10   | 4.8 (4.0)    | 8.2                      |
| Total  | 143  | 96   | 15   | 4.0 (4.0)    | 8.1                      |
| P-value|      |      |      | P = 0.013    | P = 0.904                |

**TABLE 2**  CAM utilization of MS patients

| Therapy                        | Total | After onset | During course of disease | Current utilization | % of CAM user |
|--------------------------------|-------|-------------|--------------------------|---------------------|---------------|
| Exercise therapy               | 187   | 6           | 55                       | 126                 | 79.6          |
| Vitamins                       | 127   | 4           | 55                       | 68                  | 42.2          |
| Minerals and other supplements | 108   | 0           | 50                       | 58                  | 38.8          |
| Phytotherapy                    | 83    | 3           | 37                       | 43                  | 31.1          |
| Relaxation techniques           | 80    | 2           | 37                       | 41                  | 33.0          |
| Massage                        | 60    | 4           | 33                       | 23                  | 27.7          |
| Traditional chinese medicine    | 43    | 4           | 30                       | 9                   | 19.4          |
| Homeopathy                     | 35    | 7           | 21                       | 7                   | 16.5          |
| Diets                          | 33    | 2           | 19                       | 12                  | 14.6          |
| Thermo- and hydrotherapy       | 30    | 2           | 21                       | 7                   | 13.6          |
| Electrotherapy                 | 25    | 2           | 18                       | 5                   | 11.7          |
| Hippotherapy                   | 23    | 18          | 18                       | 5                   | 11.2          |
| Occupational therapy           | 21    | 1           | 4                        | 16                  | 10.2          |
| Psychotherapy                  | 19    | 2           | 12                       | 5                   | 9.2           |
| Cannabis                       | 17    | 2           | 11                       | 4                   | 7.8           |
| Therapeutic touch              | 16    | 13          | 3                        | 6                   | 6.3           |
| Magnetic field therapy         | 14    | 1           | 8                        | 5                   | 6.8           |
| Enzyme therapy                 | 13    | 1           | 8                        | 4                   | 6.3           |
| Feldenkrais                     | 11    | 3           | 8                        | 5                   | 5.3           |
| Chiropractic medicine          | 7     | 4           | 3                        | 3                   | 3.4           |
| Gemstone therapy               | 7     | 4           | 3                        | 3                   | 3.4           |
| Amalgam removal                | 6     | 6           | 6                        |                     | 2.9           |
| Hematogen oxidation therapy    | 6     | 4           | 2                        |                     | 2.9           |
| Cobra toxin                    | 6     | 3           | 3                        |                     | 2.4           |
| Total                          | 991   | 44          | 480                      | 467                 |               |

(RRMS), 37.8% from secondary progressive (SPMS), and 5.9% from primary progressive MS (PPMS). See Table 1.

2.2.2  Statistical analyses

Descriptive analysis was performed for CAM use. MANOVA was performed to assess differences in coping behavior. In case of non-normal distribution (ie, depression score), Mann-Whitney U Test and the Kruskal-Wallis test was utilized, respectively. All statistical analyses were performed with the Statistical Package for Social Science (SPSS, version 18.0).

3  RESULTS

A total of 206 MS patients (81.1%) reported that they had used one or more unconventional therapies after diagnosis of MS. On average 4.8 different therapies were applied by users (SD±2.6).
Two-thirds made use of these therapies complementary to conventional treatment, 16.0% applied alternative therapies solely, and 18.0% reported alternative as well as complementary treatment since onset of MS. Exercise therapy, vitamins, minerals and other dietary supplements, phytotherapy, and relaxation techniques were the most frequently used CAMs (Table 2). Two-thirds of the patients were currently using CAM.

### 3.1 | Clinical and socio-demographics

The sex of patients did not have significant influence on CAM utilization (P = 0.225). Neither higher school education, nor completed professional education had significant impact on CAM utilization (P = 0.085 and P = 0.093, respectively). Whereas the net income did not influence CAM utilization (P = 0.660), current paid employment status did (P = 0.026). Religious confession (P = 0.938) or marital status (P = 0.915) were no differentiating factor between patient cohorts. CAM users (median EDSS 4.0) had a higher EDSS than nonusers (median EDSS 2.0). Similarly, disease duration was longer for CAM users (8.3 years) than for nonusers (7.3 years, P = 0.028).

### 3.2 | Coping behavior

CAM users and nonusers differed significantly in their coping behavior (P = 0.035). "Rumination," "search for information and exchange of experience," and "search for support in religion" were ascribed to a higher extent to CAM users than to nonusers. No differences were found on the remaining two coping scales (Table 3).

### 3.3 | Influence of depression

Most patients (95%) did not meet the criteria for depression. The mean BDI-score for all patients was 6.7 (median=5.0, SD±6.5). The score was positively correlated with coping scales "rumination" (r = 0.458; P < 0.001) and "search for information and exchange of experience" (r = 0.152; P = 0.032). Females showed significantly higher scores on scales "search for information and exchange of experience" (28.8 vs. 26.1, P = 0.012) and "search for social integration" (36.6 vs 34.5, P = 0.030)

### DISCUSSION

CAM is applied by a large number of MS patients during disease course with more widespread use over the last years ranging from 33% up to 70%. In our study, MS patients use CAM to an even higher extent (81.1%).

In contrast to published studies, we could show that neither sex, higher school education, completed professional education nor net income, marital status, and religious confession had significant

| Statistical Variable | Nonuser⁴ | User alternative therapies | User complementary therapies⁴ |
|----------------------|----------|----------------------------|-------------------------------|
| M                    | 5.4      | 6.2                        | 7.4                           |
| SD                   | 6.0      | 5.0                        | 6.8                           |
| Mdn                  | 4.0      | 5.0                        | 6.0                           |
| Mean rank            | 106.0    | 124.7                      | 132.5                         |

⁴Differences between nonusers and users of complementary (but not for user of alternative therapies) therapies were significant (Mann-Whitney U test; P < 0.05 after Bonferroni adjustment).
effect on the probability of CAM utilization. Only the currently paid employment status correlated positively with CAM utilization. CAM users spent approximately €1000 on average for CAM each year, thus the safety of regular income seems to be more important than net income.

CAM users had a higher EDSS than nonusers. This is in contrast to Schwarz et al\textsuperscript{13} who proposed functional independence (mirroring lower EDSS) in CAM users. Other studies showed a correlation with disease duration and severity of impairment in MS\textsuperscript{22} and non-MS patients.\textsuperscript{12,23} Similar contradictory results have been found for coping behavior in MS patients. Research revealed that coping strategies varies with the level of impairment. Patients with EDSS between 3.0 and 6.0 change their coping behavior, and tackle more intensively with their disease.\textsuperscript{8} In our cohort, CAM users (median EDSS 4.0) were more progressed than nonusers (median EDSS 2.0). CAM users differed significantly from nonusers with higher values for coping styles for "search for information." Similar interrelationships were shown for CAM utilization in oncological patients and in patients with gastroenterological and cardiologic problems.\textsuperscript{24}

One possible explanation could be that patients may notice impairment in daily life— for example, at work—and recognize that commonly utilized therapeutics might not be sufficient to halt disease progression. Thus, patients might look outside the box and go for complementary or alternative therapies.\textsuperscript{25} It is known that patients with chronic and life-threatening conditions, for example, HIV patients\textsuperscript{26} use CAM more often than control groups. It is not elucidated whether MS patients might change their CAM utilization behavior with severity of disease, although changes in the coping behavior might be an indicator for it.

The "search for information and exchange of experience" was more often reported by female MS patients, but overall no significant gender effects were seen on CAM utilization. Similarly, "search for social integration" did not affect CAM utilization. The more frequent use of this coping style by women is a gender-specific effect and similar results have been reported by McCabe and colleagues,\textsuperscript{10} who found that women are more likely to use coping strategies that involved "seeking social support" and "focusing on the positive" than men.

The more frequently reported coping style "rumination" by CAM users might be a possible indicator for a higher risk of depression in CAM users. "Rumination" seems to be correlated with depression.\textsuperscript{27}

Utilization of CAM could be interpreted as implication of emotional distress. Indeed, we found higher depression scores in users than in nonusers. Recently, the relation between integrative/alternative medicine and depression was shown in a large cohort in the United States.\textsuperscript{28} Patients might try to compensate the distress, and aim for emotional balance using CAM.\textsuperscript{8}

The coping style "search for support in religion" was ascribed to CAM users in our study more frequently than to nonusers. Similar results were shown in a recently published study.\textsuperscript{29} Religious coping can influence adaptation to stressful life events positively and negatively depending on the respective approach.\textsuperscript{29,30} A meta-analysis supported the hypotheses that positive forms of religious coping (eg, search for support by a priest) and negative forms (eg, punishment by God) are related to positive and negative psychological adjustment to stress.\textsuperscript{31} Religion has been utilized for coping since centuries with more or less unexplainable effects.\textsuperscript{31} More detailed assessment of religious coping strategies and distinct cultural particularities should be stronger taken into account in future research.

In our study, CAM users had higher depression scores than nonusers. Research in the general population indicates that CAM users are more often suffering from depression than nonusers.\textsuperscript{32} The high rate of comorbidity of depression and anxiety disorders among MS patients\textsuperscript{33} could be one cause for the frequent use of CAM in MS. The results underline the need for assessment of psychological variables and mental disorders when investigating CAM utilization.

Most important, 57.6\% of CAM users reported an improvement on their health status, whereas 40.4\% did not see any effect, and only 2\% reported a deterioration of their situation. Although not aim of our study, possible explanation might be—besides the placebo effect—the perception of having influence on the disease. The psycho-neuro-immunological relationships have not been elucidated so far, but might be an interesting future field of research.\textsuperscript{34}

## 5 | CONCLUSION

The generalizability of the results is limited by the un-matched and un-controlled design of the study. However, the study will warrant some needed insights in the use of CAM in MS patients. CAM is a widely used in MS patients—even more often than glucocorticosteroids\textsuperscript{35}, and positive effects are seen in about 60\%. Patients are willing to spend relatively high amounts of money. CAM users and nonusers differ significantly in their coping behavior. Users showed higher rates on depressions scales than nonusers and were more disabled. More research is needed to understand the effects and the inner drive for CAM. In our study, patients with mild or moderate impairment were included predominantly. Future research has to elucidate the influence of disease severity on the use of CAM. Additionally, future research has to highlight how new and more effective medication and possible side effects will influence CAM utilization.

## CONFLICT OF INTEREST

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