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Group Therapy for Patients with Mild Cognitive Impairment and Their Significant Others: Results of a Waiting-List Controlled Trial

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Mild cognitive impairment · Psychotherapy · Psychoeducation · Group therapy · Controlled clinical study · Neuropsychology

Abstract
Background: Patients with mild cognitive impairment (MCI) have to deal with an uncertain prognosis and also face a multitude of memory-related problems and psychosocial consequences. A newly developed group programme proved to be feasible, however, it needed confirmation by a controlled study. ***Aim:*** This controlled study evaluates this group therapy for MCI patients aimed to help them accept and manage the memory problems and the psychosocial consequences. The programme combines elements from psychoeducation, cognitive rehabilitation and cognitive-behavioural therapy. ***Patients and Methods:*** Ninety-three MCI patients received treatment, with 30 patients being first assigned to a waiting list, thus serving as their own control group. Pre- and post-treatment acceptance and helplessness were assessed using subscales of the Illness Cognition Questionnaire, while distress and general well-being were gauged with the Geriatric Depression Scale and subscales of the RAND-36. ***Results:*** Linear mixed model analyses showed that, relative to the controls, acceptance had increased more in the intervention group compared to the waiting-list period ($p = 0.034$). Distress and general well-being showed no changes. Treatment responders demonstrating a clinically significant effect on acceptance and two of three secondary outcome measures had higher baseline levels of helplessness and fewer self-reported memory complaints in daily life than patients who did not improve. ***Conclusion:*** The intervention helped the patients deal better with their uncertain future in that they were overall better able to accept their condition, with especially the female patients showing a decrease in helplessness cognitions, although the effects were relatively small.

Introduction

Mild cognitive impairment (MCI) is characterized by cognitive deficits in the context of normal daily functioning [1, 2]. It is a known risk factor for the development of dementia, with prospective longitudinal studies report-

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ing annual MCI-dementia conversion rates of 6% to up to 25% [3, 4]. These rates also imply that for a large proportion of MCI patients the progression of their illness is uncertain, and that the diagnosis may, rather than diminish their feelings of uncertainty, even exacerbate them. Although MCI patients can by definition still function independently in everyday life, they do encounter a multitude of difficulties because of the mild cognitive changes, inducing profound stress, which, in turn, causes more practical, social and psychological problems [5, 6]. In line with these findings, Hwang et al. [7] showed that the incidence of mood disorders, such as dysphoria, anxiety, restlessness or irritability, was higher in MCI patients than in healthy age-matched controls. To date, there is no targeted pharmacological treatment for MCI, but there is increasing evidence supporting an important role for non-pharmacological interventions in diminishing distress or disturbed behaviour in early dementia. Such interventions commonly combine elements from cognitive training, neuropsychological rehabilitation with occupational therapy, psychoeducation and psychotherapy [8]. While psychoeducation and psychotherapy are predominantly offered to the patients' caregivers, recent studies in patients with early dementia have shown that these therapeutic interventions are also feasible and effective in the patients themselves [9]. Furthermore, in a meta-analysis of psychosocial interventions for dementia, Brodaty et al. [10] found that success was more likely if both the patients and the caregivers were actively involved in the programme.

Since MCI typically is a chronic condition, for some reflecting the early stage of dementia, it is crucial to support the patients in the actual problems they encounter in daily life and to prepare them for future difficulties. Although an earlier Cochrane Review [11] did not find support for the use of cognitive rehabilitation and training interventions in patients with MCI, a recent review [12] reported positive findings for such programmes in six of the seven studies evaluated. In this review, it was recommended to combine cognitive training with interventions addressing psychosocial, attributional or self-regulatory factors. Although dedicated psychotherapeutic interventions for MCI are lacking, equipping patients with strategies to cope with the demands of the condition in an early stage of a chronic disease are thought to lie at the heart of self-management [13, 14]. In a study on the adaptation process in patients after the onset of Alzheimer's disease, a balanced struggle with acceptance in order to integrate the changes with the patients' identities was reported [15]. Here, illness acceptance was described as the outcome of a gradual process in which denial of the symptoms and facing them are interchanged in order to keep the previous 'sense of self'. In patients with chronic conditions, illness acceptance can be described as the acceptance of loss, the ability to tolerate the unpredictable and uncontrollable nature of the disorder, and coping with the aversive consequences [16]. A growing body of studies highlight the role of illness cognitions in the adaptation process and provide evidence that acceptance is related to increased psychological well-being and higher quality of life. In addition, acceptance can be increased by psychoeducation about the illness and the adaptations to the consequences of the illness in the personal life [17].

In a previous pilot study on 22 MCI patients, we introduced and tested the feasibility of a newly developed psychotherapeutic intervention for MCI patients and their partners [9]. We based our intervention on principles from cognitive-behavioural therapy (CBT) and combined these with psychoeducational and memory-rehabilitation elements. We choose CBT as the psychotherapeutic method, because CBT has been found feasible for MCI patients [17] and has been successfully applied in other cognitively impaired patient groups [18, 19]. The pilot study showed the programme to be applicable in this population, yielding promising results, with the programme contributing to the patients' acceptance of their memory impairment and showing a trend for increased marital satisfaction. The acceptance effect was related to the patients' educational level and their pre-treatment memory performance: lower levels of education were associated with a greater positive change in acceptance. Moreover, the high attendance rates suggested that the intervention clearly fulfilled a need for assistance and information felt by many MCI patients. However, the study lacked a control group, limiting the value of our findings. Also, the intervention had not diminished the level of self-reported distress, although we suggested this was because of the already low pre-treatment levels.

The main aim of the current study was to demonstrate the effectiveness of our group CBT programme for MCI patients and their partners/caregivers in a controlled design and in a larger patient sample. Based on our pilot data and other empirical evidence suggesting that acceptance plays a crucial role in coping with chronic medical conditions, we adopted 'acceptance' as the primary outcome measure in the current trial. We hypothesised that this variable would increase significantly more after the intervention compared to a waiting-list period. Since pa-

tient characteristics such as age, sex, and educational level may sometimes be more important than disease-related variables [21], we also explored the changes in acceptance in relation to six pertinent patient factors, i.e. age, sex, educational level, cognitive status, coping behaviour, and perceived social support. In addition, we evaluated well-being, distress and feelings of helplessness, expecting helplessness to be reduced due to the psychoeducation and coping strategies offered in the programme. Since the primary outcome measures, the nature of the experienced difficulties with the MCI diagnosis and the expected coping mechanisms differ between the patients themselves and the significant others, we report the findings of the latter group in a separate paper.

Patients and Methods

Patients

Between September 2003 and December 2007, eligible MCI patients and their significant others from four regional outpatient memory clinics in the east of the Netherlands offering the treatment were recruited (i.e. Radboud University Nijmegen Medical Centre and three general hospitals, viz. 'Maasziekenhuis Pantein' in Boxmeer, 'Rijnstate' in Arnhem and 'Slingeland' in Doetinchem). Inclusion criteria were an MCI diagnosis, that is, amnestic MCI, non-memory single-domain MCI or multiple-domains MCI [2], age over 50 years, and the availability of a partner/spouse, relative, or close friend willing to participate in the study. In all four participating centres, MCI was diagnosed using a multidisciplinary approach supervised by a geriatrician or neurologist, according to generally accepted criteria described by Petersen [1, 2]. This approach consisted of a thorough clinical interview with the patient dyads, supported by an extensive neuropsychological assessment, neurological and radiological findings and assessment of activities of daily living. Performance on the neuropsychological tests was rated as falling within the normal range, below average, or impaired as based on available age- and education-adjusted normative data, with performance between 1 SD below or above the normative mean being defined as normal, between –1 SD and –1.65 SD below the normative mean as below average, and more than –1.65 SD below the normative mean as impaired [22]. The MCI criteria were met if a patient's performance was impaired in one of the cognitive domains, or if more than one cognitive domain showed his/her performance to be below average, all in the absence of a decline in activities of daily living or dementia. Instrumental activities of daily living were assessed using validated rating scales (such as the Lawton Instrumental Activities of Daily Living Scale [23]) and/or by structured observation of daily-life activities by an occupational therapists (either in the patient's home environment or in the outpatient clinic). The clinical diagnosis was decisive in cases in which the neuropsychological performance outcomes did not correspond with the clinical impression. Participants were excluded if they fulfilled the criteria for dementia. Other exclusion criteria were the absence of informed consent, the presence of psychiatric co-morbidity, co-existing somatic disorders if dominant to MCI, severe concentration difficulties impeding communication, inability to communicate fluently in Dutch, lack of motivation to share experiences in a group, and evidence of severe, pre-existing partner relationship problems unrelated to the cognitive impairments.

Study Design and Procedure

The study had a naturalistic, non-randomized, waiting-list controlled design, with all eligible patients receiving the group treatment either within 8 weeks of their recruitment or after having first spent 8 weeks or more on a waiting list (waiting for a new intervention group to begin). The patients receiving treatment within 8 weeks of the intake interview, the 'intervention-only' group, were first assessed in the 2 weeks prior to their treatment (T1) and within 2 weeks after treatment completion (T2). When the time to the start of the next group intervention was more than 8 weeks, patients were assigned to a waiting list, serving as our control group, at the start of which period they took a baseline assessment (T0), with their pre-treatment (T1) test also scheduled within 2 weeks before the start of their group and the post-treatment test within 2 weeks after treatment completion (T2). To maximize the statistical power, the total intervention group we report here is hence composed of patients having received 'immediate' treatment and those having received treatment after a waiting-list period.

The patients meeting the inclusion criteria were informed about the group intervention programme by their geriatricians or neurologists. Interested patients were subsequently invited with their significant others for an interview with a psychotherapist at their local hospital, who explained them the aims and content of the group programme and obtained their written, informed consent. By exploring the expectations the patients and their significant others had of the programme, which were corrected when these were unrealistic, the therapist estimated the participants' potential capability and interest in the group programme. All subsequent assessments were conducted by trained psychology (research) assistants of the hospital delivering the intervention. Patients received no other psychosocial or medical intervention for their cognitive impairment during the waiting list or intervention interval.

Demographic Variables and Patient Characteristics

Demographic variables, such as age, sex, marital status and education level, were assessed with a general checklist. Participants rated their educational level on a 7-point scale with 1 reflecting less than primary school (<6 years of education), and 7 a university degree (Bachelor degree and up: >14 years of education) [24, 25].

In the patients, *overall cognitive impairment* was estimated with the Mini-Mental State Examination (MMSE) [26], which gives an overall impression of the cognitive decline. Memory function was assessed with the Dutch version of the Rey Auditory Verbal Learning Test [27], which requires the participant to recall 15 orally presented words in 5 trials, immediately after their presentation and after a 20-min delay, followed by a recognition trial in which the 15 words are presented among 15 distracter items. Since the delayed recall measure is an early predictor of cognitive decline [27, 28], we used this measure as an index of episodic memory performance.

Coping was assessed with two subscales of the Utrecht Coping List (UCL) [30] gauging active and passive coping strategies when dealing with everyday problems. The 7-item Active Coping subscale evaluates cognitive and behavioural efforts to apply goal-oriented problem-solving strategies and the 8-item Avoidance subscale cognitive and behavioural attempts to avoid, escape from and acquiesce when facing everyday problems.

Subjective memory decline was investigated by having the patients complete the 16-item Dutch patient version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE-N-Pt) [31–33], the instructions of which were slightly adjusted [9]. The respondent rates his/her memory decline in daily life relative to his/her daily memory functioning about 10 years before, on a 5-point scale ranging from 'Much improved', (1 point) to 'Much worse' (5 points) with a score of 3 reflecting 'No change'.

Social support in the past 2 weeks was evaluated with the 12-item Social Support List, Interaction version (SSLI-12), an inventory designed for use in elderly people, which consists of three 4-item subscales: Everyday social support (SSLI-EV), Social support in problem situations (SSLI-PR), and Esteem support (SSLI-EST) [34].

Outcome Measures

Acceptance was the primary outcome measure and assessed with the Illness Cognition Questionnaire (ICQ) [16], which assesses the way patients cognitively adjust to their chronic condition. Acceptance is one of its three subscales and has 6 items that assess the patients' recognition of the need to adapt to their chronic disease and their ability to tolerate and manage its adverse consequences (e.g., 'I have learned to live with my memory problems'; 'I think I can handle the problems related to the memory problems, even if they get worse').

The subscale scores can range from 6 to 24 with higher scores reflecting more cognitions of acceptance.

Distress was evaluated as one of three secondary outcome measures by means of the 15-item Geriatric Depression Scale-Short Form (GDS-15) [35], with higher scores reflecting more depressive symptoms (with 5 being the cutoff score for depressive symptoms).

General well-being was assessed using the Dutch version of the RAND-36 Health Survey [36], which measures physical, social and emotional dimensions. We used four of the eight scales, i.e. Social Functioning, Role-Emotional, Mental Health, and Vitality. Each scale ranges from 0 to 100, with higher scores reflecting higher levels of perceived health or well-being.

Helplessness was evaluated with the same-named subscale of the ICQ [16], which focuses on the adverse aspects of the disease and generalizes them to daily functioning. The 6-item subscale ranges from 6 to 24, with higher scores reflecting more feelings of helplessness.

Intervention

The intervention consisted of ten weekly 2-hour group sessions and was based on CBT principles combined with psychoeducational and memory rehabilitation elements. The programme and procedures have been extensively described elsewhere [9]. Each group comprised 5–8 patients all accompanied by a significant other, i.e. a partner, adult child, relative or close friend. The focus of the programme was the acquisition of knowledge of and skills to adequately cope with MCI-associated symptoms and their consequences. Slight adjustments in the CBT method, like shortening of verbal or written instructions, repeating important information or personal goals and using of reminder cues, requiring the patient to make notes, or simply repeating the ongoing discussion, were made because of the cognitive impairments of the patients [19, 37]. The therapists delivering the treatment were all registered psychologists trained and supervised by the first author.

To promote mutual support among the participating patients and between the patients and their significant others, we implemented the procedure described by Snyder et al. [38] in that the first 90 min of each 2-hour session the patients and their partners participated in separate groups, that is, a patient and a 'partner' group, each with its own therapist, both groups exploring the same topics and receiving similar (oral and written) information with relevant home assignments. For the remaining 30 min, the two groups came together and the key issues from the preceding session were summarized and highlighted.

Participants learned to optimize internal and external memory strategies, to recognize memory problems in daily life and to explore their explanations and attributions, improve the communication with their partner and others and train self-regulation skills. Topics such as diagnostic uncertainty, dependency on others and stigmatization were discussed in relation to each theme. All participants were instructed to prepare each session with relevant texts and self-monitoring tasks. The patients were asked to monitor their thoughts, feelings and behaviour in situations of cognitive failure or stress, with the aim to reduce or prevent irrational and stress inducing cognitions. The following topics were addressed: memory function in general, MCI as a clinical diagnosis, therapeutic possibilities, strategies to improve memory performance (such as note taking, errorless learning and using a memory book), ways to recognize strain, learning to relax, the importance of pleasant everyday activities, and dealing with social conflicts and worrying.

Statistical Analyses

Baseline differences between the waiting-list group and the intervention-only group were analyzed by independent samples t tests. To analyze changes in the two dependent distress variables and the two illness cognition outcomes following the waiting-list and intervention interval, we applied a linear mixed model (LMM) for repeated measurements. We opted for LMM because this approach, in comparison to repeated-measures analysis of variance, does not require data to be present at each assessment time point for a participant to be included in the statistical analysis whilst at the same time accommodating the dependency caused by repeated measurements. In the outcome variables, differences between T0 and T1 (change after waiting-list interval), and between T1 and T2 (change in intervention interval) were calculated and used as repeated measures with interval (2 levels), group (17 levels), sex (2 levels) and their first-order interactions as fixed factors. We included sex as a fixed factor because we assumed it might be an important factor, influencing outcome. To correct for potential group effects, we introduced Group as a fixed factor into the analysis. Interval (T0-T1 vs. T1-T2) was entered as a within-subject variable. We used the procedure MIXED from the SPSS package (version 14).

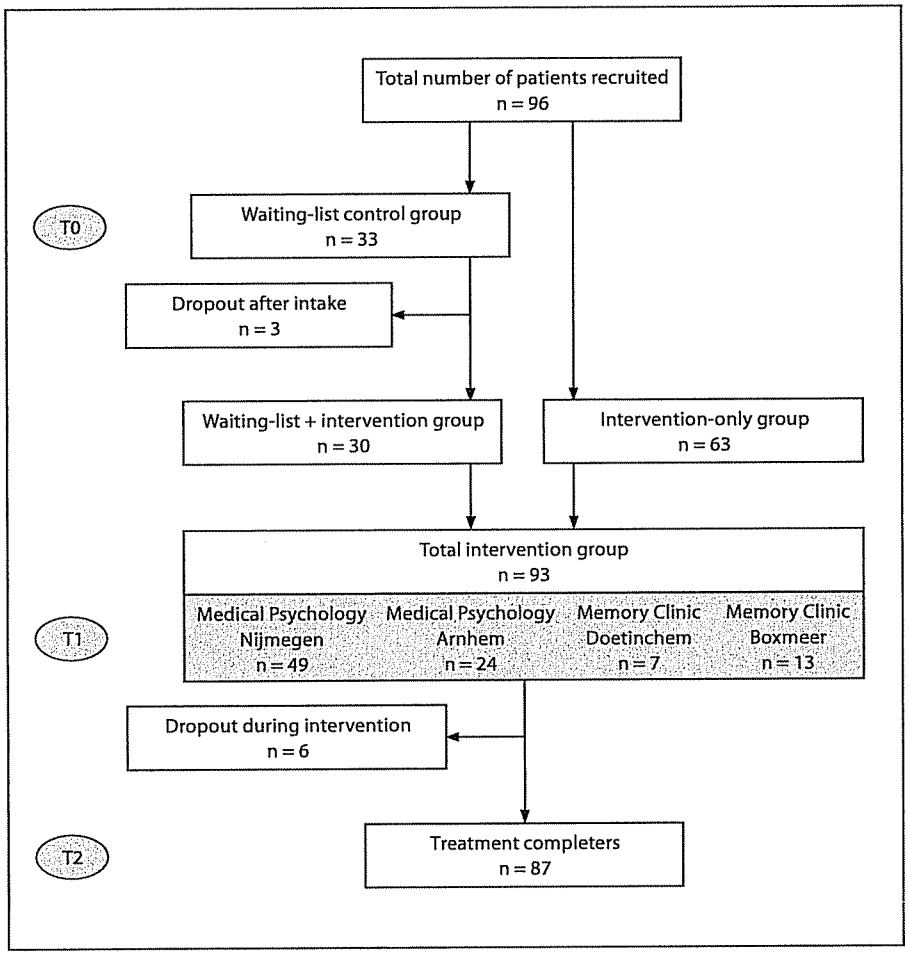

Fig. 1. Flow chart showing the assignments of the patients to the waiting-list + intervention and the intervention-only group.

The power calculation we ran in our pilot study had indicated that approximately 70 patients were required to reach a power of 0.8, with a significance level of 0.05 [9].

Finally, we performed an exploratory responder analysis to describe the characteristics of the patients who had benefited (most) from the intervention. To this end, patients were categorized as responders when we obtained an effect size >0.2 in the intervention interval on ICQ Acceptance, the primary outcome, and an effect size of at least >0.2 on two of the other three secondary outcome measures (GDS-15 Distress, RAND-36 General well-being and ICQ Helplessness). Effect sizes (Cohen's *d*) were computed based on the differences between pre- and post-intervention means and the pooled variance [39]. Following Cohen, we took an effect size of 0.2 to reflect a small but significant clinical effect. The participants not meeting these criteria were categorized as non-responders. Differences between the effect sizes of the two conditions were tested with Student's t test. For the group comparison of the patient characteristics obtained at T1 (pre-treatment), we used an ANOVA in which responder group is the grouping variable and the patient characteristics data the dependent variables.

Results

Ninety-six MCI patients expressed an interest to participate in our trial and were included (see fig. 1 for a trial overview).

The intake of 33 dyads took place more than 9 weeks before the start of a new intervention group and they were hence first placed on the waiting list, constituting our control group, with 3 dyads dropping out after the baseline (T0) assessment because of (1) medical illness or (2) lack of time. The other 63 patients started treatment within 8 weeks of their intake interview, accordingly constituting the 'intervention-only' group. Thus, a total of 93 patients, i.e. 30 patients from the waiting-list group and 63 patients from the 'intervention-only' group, were assessed at T1 (pre-treatment). The intervention-only group was twice the size of the control group due to the variability in the flow of referrals in the four participating hospital and the study schedule. Of the final intervention

Table 1. Baseline characteristics of the patients in the two study groups

	Waiting-list group (n = 30)	Intervention-only group (n = 63)	p
Demographics			
Age	69.4 (7.2)	70.5 (7.0)	0.51
Education (1 = low, 7 = high)	4.9 (1.2)	5.0 (1.1)	0.78
M/F*	14 M (47%)/16 F (53%)	34 M (53%)/29 F (47%)	0.24**
MMSE	25.8 (3.9)	25.6 (3.2)	0.86
Type of partner*			0.65**
Married/living together	27 (90.0%)	57 (90.4%)	
Living apart	3 (10.0%)	1 (1.6%)	
Daughter/sister	0	5 (8.0%)	
Patient characteristics			
RAVLT – Delayed recall	2.9 (3.5)	2.7 (2.2)	0.79
SSLI – EV	10.3 (1.8)	10.8 (1.9)	0.29
SSLI – PR	9.6 (2.5)	9.1 (2.8)	0.41
SSLI – EST	9.4 (2.7)	9.5 (2.9)	0.88
UCL – Active coping	15.6 (4.7)	16.8 (3.4)	0.17
UCL – Passive coping	16.7 (3.7)	17.0 (3.3)	0.70
IQCODE-N-Pt	58.1 (7.2)	57.2 (8.5)	0.63
Dependent variables			
GDS-15 (cutoff = 5)	3.6 (2.8)	3.0 (2.2)	0.27
GDS-15 >5	16.7%	14.5%	
RAND-36	261.7 (73.3)	287.0 (65.4)	0.10
ICQ Acceptance	13.4 (4.0)	13.5 (4.0)	0.90
ICQ Helplessness	10.2 (2.2)	11.2 (3.1)	0.12

MMSE = Mini Mental State Examination; RAVLT = Rey Auditory Verbal Learning Test; SSLI = Social Support List Interaction-version; EV = everyday social support; PR = social support in problem situations; EST = esteem support; UCL = Utrecht Coping List; IQCODE-N-Pt = Informant Questionnaire on Cognitive Decline in the Elderly – Dutch patient version; GDS-15 = Geriatric Depression Scale-Short Form; ICQ = Illness Cognition Questionnaire Acceptance and Helplessness Scale. Data represent means (SD) or * = numbers of patients, unless otherwise indicated. All p values refer to Student's t tests, except ** = Mann-Whitney U test.

Table 2. Effect sizes (ES) with standard deviations (SD) and means with SD in the outcome measures

Outcome measure	Mean ES waiting-list interval (SD)	Mean ES intervention interval (SD)	T = 0 (n = 30)	T = 1 (n = 93)	T = 2 (n = 87)
GDS-15	0.16 (0.9)	–0.04 (1.0)	3.57 (2.8)	3.05 (2.3)	3.11 (2.6)
RAND	0.14 (0.7)	0.12 (0.3)	261.7 (73.3)	281.6 (68.2)	282.2 (75.9)
Acceptance	0.08 (0.8)	0.34 (0.9)	13.40 (4.0)	13.62 (4.3)	15.25 (4.7)
Helplessness	0.03 (0.8)	0.23 (0.9)	10.20 (2.2)	10.89 (2.9)	10.29 (2.9)

GDS-15 = Geriatric Depression Scale-Short Form.

group (n = 93), no post-treatment (T2) data were available for 6 patients who left the treatment prematurely. Reasons for discontinuation were the occurrence of serious medical problems unrelated to the MCI (n = 4) and loss of motivation (n = 2). The patients dropping out did not differ from the completers with respect to the patient characteristics and baseline outcomes, although relatively more dropouts lived alone. Thus, the data of 87 patients entered the LMM analyses.

Baseline Patient Characteristics

Table 1 lists the patients' baseline data for the two study groups (T0 and T1, respectively). Between-group comparisons revealed no significant differences in their demographics (age, education, relationship to study partner), main characteristics (MMSE, coping style, social support, and subjective memory deterioration) nor primary or secondary outcomes, measured at baseline.

Treatment Effects

Table 2 shows the means of the outcome measures at pre- and post-treatment assessments and the effect sizes for the patients in the waiting-list and the intervention intervals.

The LMM analysis revealed a significant difference between the two conditions for our primary outcome measure of Acceptance ($F(1,63.8) = 4.7$, $p = 0.034$) with an estimated difference between the two conditions of 3.49 and a 95% confidence interval ranging from −6.21 to −0.73 (d.f. = 73.1, $p = 0.014$). Estimated mean changes for Acceptance are −0.99 (SE = 0.9) in the waiting-list interval and 1.2 (SE = 0.4) in the intervention interval. This reflects an increase in pre- to post-acceptance during the intervention interval relative to the values obtained during the waiting-list interval, with effect sizes of at least 0.2 being obtained for 51% of the patients. As to the secondary measures, Helplessness showed an interaction effect between intervention and sex ($F(1,80.9) = 4.95$, $p = 0.029$), while no main effects were found for Distress ($F(1,45.3) = 0.93$, $p = 0.34$) and General well-being ($F(1,44.6) = 0.08$, $p = 0.78$).

To explore the possible confounding effect of the waiting-list interval on the subsequent intervention, the means of the acceptance at the three assessment moments for the waiting-list group and the intervention-only group are shown separately in figure 2. No statistical differences were found between the intervention-only group and the waiting-list plus intervention group at either T1 $t(89) = 1.09$, $p = 0.91$ or T2 $t(86) = 1.33$, $p = 0.19$, indicating that the effect in the participants who were assigned to the waiting-list interval before receiving the actual intervention did not show a differential effect compared to the group who received the intervention immediately after recruitment.

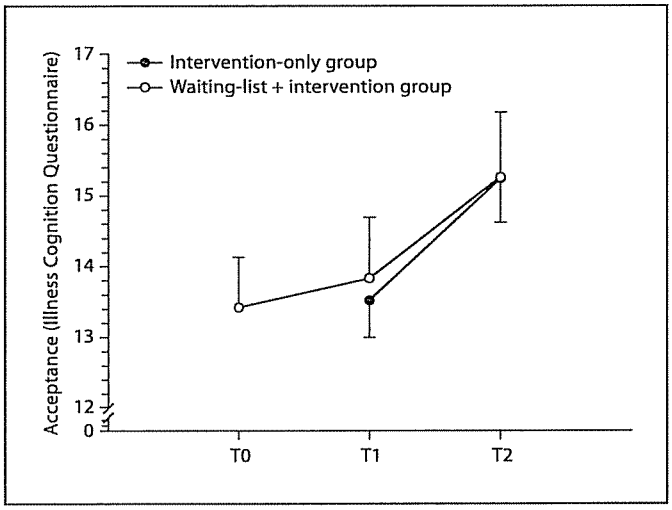

Fig. 2. Mean acceptance scores (+SEM) for T0, T1 and T2 for the waiting-list + intervention and the intervention-only group separately.

Table 3 lists the mean change in Helplessness as a function of sex, revealing an inverse direction for the two intervals for the female patients, reflecting a decrease in helplessness following the intervention. No such direction of change was found for the male patients.

Responder Analysis

Comparing the patient characteristics and baseline scores on the outcome measures of the treatment responders (n = 24, 36.2%) and the non-responders (n = 63; see table 4), we found a difference for Helplessness ($F(1,85) = 4.9$, $p = 0.029$), with the responders showing higher levels of helplessness than the non-responders. Perceived memory problems (IQCODE-N-Pt) and education level both showed a trend ($F(1,83) = 2.9$, $p = 0.089$ and $F(1,85) = 3.0$, $p = 0.092$ respectively), with responders reporting slightly fewer memory problems and lower levels of education than the non-responders.

Discussion

In this first controlled study of a comprehensive group therapy for patients with MCI and their significant others, we confirmed the hypothesis we formulated on the

Table 3. Estimated marginal means (and standard errors) for changes in Helplessness as a function of sex for the waiting-list and the intervention interval

	Change waiting-list interval	d.f.	Change intervention interval	d.f.
Women	0.77 (0.72)	97.4	−1.06 (0.82)	91.32
Men	−1.10 (0.46)	94.9	−0.27 (0.40)	93.48

Negative means indicate that helplessness cognitions decreased, while positive means reflect an increase.

Table 4. Means and standard deviations (SD) for the main differences in pre-treatment variables for the treatment responders and non-responders (full patient sample)

	Responders (n = 24)	Non-responders (n = 63)	p
Education	4.7 (1.0)	5.1 (1.0)	0.087
Helplessness	12.0 (3.4)	10.4 (2.6)	0.029
IQCODE-N-Pt	55.3 (9.0)	58.4 (7.1)	0.092

IQCODE-N-Pt = Informant Questionnaire on Cognitive Decline in the Elderly – Dutch patient version.

basis of our pilot study [9] that following our dedicated treatment patients would be more accepting of their condition (as assessed with the ICQ) than their counterparts awaiting treatment. Improving the patients' acceptance is crucial since MCI comes with a relatively high degree of uncontrollability and unpredictability and acceptance allows an optimal adaptation to this uncertain condition. In their validation study of the ICQ, Evers et al. [16] postulated that acceptance reflects a cognitive evaluation of the perceived ability to live with and master the aversive consequences of a condition and they indeed found that higher levels of acceptance were related to superior psychological health and coping skills. With respect to coping behaviour, recent studies have indicated that the onset of dementia places major demands on a person's coping resources [40], and it can be argued that the same holds for MCI patients.

Another interesting aspect of acceptance is that it implies an awareness of the current memory problems, underscoring its relevance in therapy given that awareness has been found to be an important predictive factor of treatment success in patients with dementia undergoing various types of therapy [41–43]. As also in MCI the patients' awareness of their condition has been found to be diminished [44, 45], increasing their acceptance necessarily raises their awareness and thus the chance of a favourable treatment outcome.

Despite the relevance of the findings supporting our pilot study [9] and thus a non-pharmacological treatment of MCI, we found again no changes on the subjective measures of general well-being (RAND-36) or distress (GDS-15). With respect to distress, scores on the GDS-15 Distress measure were already at a floor level before treatment, indicating that further reduction was not possible. These normal levels of general well-being and distress are in agreement with the study of McIlvane et al. [46]. Another explanation for the lack of change may be the relatively short intervention period (10 weeks). Reporting on a cognitive-motor intervention for patients diagnosed with MCI and mild-to-moderate Alzheimer's disease, Olazaran et al. [47] found that after 12 months of treatment, the affective status of the patients was maintained or improved compared to the control group. In conclusion, it is not unlikely that we might have obtained larger effects if the intervention had lasted longer or if we had re-assessed the patients after a certain follow-up interval. Additionally or alternatively, our 10-week intervention not only aims to help the patients and their partners/caregivers cope with the current problems resulting from the MCI, but also, or perhaps even more so, with any future consequences. Hence, changes in coping strategies and subsequent changes in perceptions of well-being may not become apparent until after 1 or 2 years. Still, the reported increase in acceptance correlated significantly with an increase in well-being ($r = 0.41$, $p = 0.003$). This is in agreement with findings in several studies indicating that acceptance plays a mediating role in adaptation to (chronic) illness resulting a higher well-being [17].

As far as we know, no other studies exist on the effect of a psychotherapy group for patients with MCI or early dementia aimed at improving acceptance. However, previous findings in patients with mild to moderate dementia after group psychotherapy [48, 49] showed a decrease in depression, and a trend for a decrease in anxiety. It is suggested that psychotherapy can be more effective on reducing levels of depression compared to psychoeducation. Moreover, a systematic review of cognitive rehabilitation programs for individuals with MCI shows only in 3 of 9 studies an amelioration of the mood, anxiety of quality of life [50]. Consequently, it can be hypothesised

that both psychotherapeutic and cognitive rehabilitation programs have effects on distress and/or well-being. With regard to our programme, combining psychoeducation, cognitive rehabilitation and psychotherapeutic elements, each part lasted only 3 sessions which may have resulted in smaller changes.

We further found a significant interaction effect between the intervention and sex on ICQ helplessness in that the attribute had decreased more in the female patients. As sex-specific coping strategies and self-reported stress have been described before in chronically ill patients [21, 51], our results were not surprising, but do provide some insight into the sex-specific coping patterns in MCI patients, which merit further investigation to allow us to adapt and optimize psychosocial interventions to these specific styles.

We also sought to delineate typical characteristics in the patients who responded to our programme. We defined responders as those patients for whom we obtained an effect size larger than 0.2 on 'acceptance' and an effect size of at least 0.2 for two other outcome measures. Our analysis revealed differences on 'helplessness', with the responders having higher pre-treatment levels of helplessness. We additionally found trends for subjective memory problems (as measured with the patient-rated IQCODE-N) and level of education, with the treatment responders reporting fewer memory problems in daily life and a lower educational level. Reported memory problems were not related to the level of memory impairment ($r = -0.11$, $p = 0.39$) which is in accordance with the findings of Jungwirth et al. [52]. Based on these results, we recommend using these easily assessed factors for the selection of patients most eligible for treatment.

Furthermore, the programme addressed topics known to pose serious problems in MCI patients [5]. However, individual differences during the intervention were considerable, which may explain why two of the three secondary outcome measures failed to show a change. The session on the theme of worrying, for example, triggered very diverse reactions: about one third of the participants confirmed they worried a lot, while one third said not to worry much or not at all. This could be a result of inter-individual differences between participants combined with the nature of the coping process in individual MCI patients in whom denial is interchanged with facing the problem and accepting it and gradually will be diminished [15]. Other topics, among which shame, stress management, social consequences, or perceived social support, showed very diverse interests too. Clearly, the format of our current group intervention was not designed to address individual problems. Tailoring the intervention by having patients with similar profiles participate in targeted programme modules, with each module lasting several sessions, may improve treatment outcome. For example, after an introductory psychoeducational module about MCI, memory and memory-enhancing behaviour, subsequent modules could either address the themes of the current programme, or could adopt a strict psychotherapeutic or cognitive rehabilitation approach. Possibly, patients with lower levels of acceptance and/or helplessness may benefit from a strict psychotherapeutic approach which focuses explicitly on sharing experiences of memory loss, reflecting on the emotional significance of participants' views on changing relationships with other people and working with behavioural experiments. Obviously, organising such a tailored programme would be a challenge because of the co-existing partner group and the aim to offer both patients and partners the same topics in order to stimulate sharing and working together.

Several methodological considerations are in order: although not a fully randomized trial, in our study the patient dyads were pseudo-randomly assigned to the waiting-list condition on the basis of the pseudo-random moment the patients were referred for treatment. Moreover, the criterion for randomization was met, because the two groups did not differ in the baseline outcome measures and patient characteristics. A limitation of this study design may be that the assessment of the effectiveness of the intervention was based on patients who received the intervention after a waiting list period and patients who received the intervention immediately after recruitment. Consequently, the waiting-list plus intervention group received an extra assessment (i.e. before the waiting-list period). Also, the waiting-list period itself may have affected the intervention outcome differentially. However, direct comparison of the two groups with respect to the intervention effect did not reveal a different pattern with respect to the main outcome variable, suggesting that our results can be interpreted validly. Also, dedicated outcome measures that evaluate the specific therapeutic goals should then be used rather than generic measures. Recently, outcome measures that specifically address areas of saliency to patient education and self-management programmes have been developed which may more accurately reflect the impact of this type of intervention [53]. The Goal Attainment Scaling proved to be useful in evaluating important aspects of psychogeriatric patients with cognitive disorders [54] and could be recommended in the evaluation of our programme.

In conclusion, our comprehensive psychotherapeutic group programme for MCI patients and their significant others yielded small, yet promising results by increasing the patients' acceptance of their condition and by decreasing feelings of helplessness in the female patients, with a third of all patients meeting conservative responder criteria for at least three of the four outcome measures. Based on the current results, we venture that the efficacy of our intervention may be improved by tailoring the content to patients sharing particular pertinent characteristics and by incorporating more sex-specific themes and training.

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