

RESEARCH ARTICLE

Awareness and cognitive rehabilitation in Alzheimer's disease and frontotemporal dementia

Eric Salmon^{1,2}  | Françoise Lekeu¹ | Anne Quittre¹ | Vinciane Godichard¹ |
Catherine Olivier¹ | Vinciane Wojtasik¹ | Christine Bastin²

¹Memory clinic, Department of Neurology, CHU Liege, Liege, Belgium

²GIGA Cyclotron Research Centre, University of Liege, Liege, Belgium

Correspondence

Eric Salmon, GIGA Cyclotron Research Centre, University of Liege, B30 Sart Tilman, 4000 Liege, Belgium.

Email: eric.salmon@uliege.be

Abstract

INTRODUCTION: Awareness influences the evolution of neurodegenerative dementias. We gathered participants' and caregivers assessments of dependence in daily activities and we studied how each score would be related to next year participant autonomy, independently of other explicative variables.

METHOD: We retrospectively analyzed data from mildly demented participants with a clinical diagnosis of Alzheimer's disease (AD, $n = 186$) and frontotemporal dementia (FTD, $n = 29$) and their relatives. A research tool was used to assess participant dependence in 98 daily activities and associated caregiver burden. A discrepancy score between the patient's and relative's judgment was calculated to evaluate awareness of dependence in activities at baseline. This dependence scores, as well as sex, age, education, and 1 year difference in Mini-Mental State Examination were taken as possible explicative variables for dependence in activities adapted by therapists during a 1-year cognitive rehabilitation program.

RESULTS: Patients with FTD showed less awareness for daily dependence (discrepancy 20.9% vs. 11.8% in AD). Both groups benefited from cognitive rehabilitation (25% decrease in dependence) and subjective burden of relatives was decreased in both groups. In the AD group, there was a significant positive relationship between both caregiver ($P < 0.001$) and participant's ($P < 0.02$) evaluation of dependence in daily activities at inclusion and dependence of participants in adapted activities after 1 year.

DISCUSSION: Awareness of impairment in daily activities is a clinical symptom that is more important at inclusion in FTD than in AD. However, in participants with AD who, as a group, significantly benefit from a cognitive rehabilitation program, not only caregiver's but also participant's assessment of dependence at baseline is correlated to subsequent, next year greater dependence in daily activities adapted by the therapists. Although discrepant, both caregiver and participant evaluations appear to be important variables to understand the evolution and the benefit of care in participants at early stages of dementia.

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KEYWORDS

Alzheimer's disease, anosognosia, autonomy, awareness, burden, cognitive rehabilitation, daily activities, dependence, frontotemporal dementia, longitudinal

1 | BACKGROUND

Awareness is a multidimensional clinical symptom frequently observed in neurodegenerative dementia, such as frontotemporal dementia (FTD) or Alzheimer's disease (AD) type dementia.¹ Patients can be more or less unaware of disturbances in cognitive, behavioral, or daily functioning. Unawareness (or anosognosia) of memory difficulties was already observed in patients with mild cognitive impairment (MCI) who progressed to AD.^{2,3} Unawareness for memory difficulties is not different in a mild stage of FTD and AD, but FTD participants are less aware of their impaired behavior and daily activities than persons with AD.⁴ High level of unawareness of clinical difficulties is related to greater caregiver's burden and poorer patients' compliance with treatment.⁵⁻⁷ A discrepancy score between a participant's and caregiver's judgment is frequently used as a measure of unawareness.⁸ Self-assessment of current capacities was rarely considered as such to predict clinical evolution in participants with dementia.⁹⁻¹¹ The objective of our retrospective analysis was to explore the relationship between initial assessment of dependence in daily activities by participants at an early stage of dementia and their caregiver and 1 year evolution of autonomy in behavioral variant (bv)FTD and AD participants who benefited from an individualized cognitive rehabilitation (CR) program. CR was rarely studied in FTD. We expected lower awareness of daily impairment in bvFTD participants. We hypothesized that caregiver evaluation of daily difficulties at baseline would be the main predictor of dependence in activities adapted by therapists during the 1-year CR program in both groups and that unawareness would influence the effectiveness of the CR program on everyday life dysfunction.

2 | METHODS

2.1 | Patients

We retrospectively assessed data from participants and their caregivers who were included in a program of cognitive rehabilitation supported by the Belgian Federal Institute for Health Insurance.¹² Their diagnosis was AD ($n = 186$) or bvFTD ($n = 29$) according to international criteria,^{13,14} with or without associated vascular brain pathology. Structural neuroimaging was used to visualize medial temporal or frontotemporal neurodegeneration. They had mild to moderate dementia according to the Mini-Mental State Examination (MMSE) obtained at inclusion,¹⁵ and they were living at home without major psychiatric disorder as assessed by the neuropsychiatrist during the diagnostic procedure. Participants agreed to try to maintain daily activities with the help of a relative. Accordingly, the level of unawareness concerning their clinical status was not severe enough to prevent them from

accepting CR. The study was approved by the university ethic committee and written informed consent to participate was obtained from the participant and his or her relative. Moreover, activities to be adapted in the CR program were mentioned in a written contract.

2.2 | Cognitive rehabilitation program

The CR program was previously described and consisted of one weekly individual session of 1 hour during 3 months at home, followed by one monthly contact for 9 months.^{12,16} Initial and follow-up (1 year) assessments were carried out for each participant and caregiver. The first step of the CR program was to evaluate difficulties in daily life activities which were important and relevant for the participant and the relative using the Profinteg research tool.¹⁷ The latter was used to determine the level of performance in 98 instrumental activities of daily living (IADL) and to identify the presence of specific difficulties reported by the participant and the caregiver. The experimental tool also evaluated the objective and subjective caregiver's burden. The second step was to select the problematic activities for which adaptation was valuable and realistic. The most frequently adapted activities in both groups were developing memory aids to remember daily tasks and appointments, kitchen or leisure activities, use of electronic devices, or adapting technologies of communication. Third, a specific program to adapt each selected activity was defined. For each activity, the program was designed according to individual difficulties in motivation or initiation, in omission of necessary steps, or in inappropriate execution at a given stage. The CR procedure used routines, such as lists, to remind daily activities of interest, written instructions describing step-by-step procedures, or verbal or visual recovery cues, depending on preserved capacities of the participant. Specific techniques were applied according to the objective, such as a spaced retrieval technique or errorless progressive adaptation to avoid improper performance. Furthermore, an adaptation of the environment was frequently required. Finally, to ensure a good practice of the activity at home, researchers explained to caregivers the procedure, the importance of maintaining the procedure as a routine and only intervening when necessary. Psychosocial counseling was also provided to relatives, such as explaining the disease, suggesting coping strategies, and help finding external leisure activities or social support.

2.3 | Evaluations

The Profinteg scale is a research tool that focuses specifically on impairment in 98 IADL due to cognitive deficits, to guide an ecological CR and evaluate progress made on these activities.^{12,16,17} There

is no cut-off value yet. The evaluation of impairment in daily activities took place after the participants had agreed to enter the CR program to improve their daily functioning. Briefly, the patient and the caregiver were asked to identify if an activity was impaired and estimate the dependence on caregiver's intervention in daily life. The total score corresponded to the severity of reported dependence, with 0 point if no difficulty and 1 point for each of the following activities: lack of activity initiation, omission of one or several steps, or wrong execution of one or several steps (maximum 3 points), 4 points corresponding to perseveration errors despite caregiver's intervention, and 5 points if the activity could not be carried out. Points were summed over all the assessed activities and expressed in percentage of the maximal dependence score. Furthermore, for each daily activity, caregivers had to evaluate the objective burden (time spent to manage patient's deficit) and subjective burden (the arduousness to assume the problematic activity or to help the patient in his or her realization) resulting from these activities (on a scale ranging from 0 to 3 for negligible, low, moderate, or high burden, respectively; points were summed over all the assessed activities and expressed in percentage of the maximal score). A baseline measure of anosognosia for impaired autonomy in daily activities was calculated as a difference between the relative's and the patient's rating of dependence (with higher positive values reflecting greater degree of anosognosia). The Zarit Burden Interview was also administered at baseline as a classical global burden measure.¹⁸ The Neuropsychiatric Inventory questionnaire was also obtained at inclusion.¹⁹ The MMSE was used to assess global cognitive deterioration.¹⁵ Education was scored as 1 = elementary school, 2 = lower secondary school, or 3 = higher education.

2.4 | Data analyses

Analysis of variance was used to analyze data obtained in the two groups at baseline and 1 year follow-up, followed by post hoc Tukey test with unequal numbers of participants. A Mann-Whitney test was used for between-group comparison at baseline. In the AD group, a multiple regression analysis assessed the association between dependence in activities adapted during the CR program at 1 year as dependent variable (our main objective) and baseline participant or caregiver global dependence score, sex, age, education, and the difference (follow-up minus baseline) of MMSE scores (the main characteristics of our sample) as predictors. In the bvFTD group, as the number of patients was too small to include several covariates in a multiple regression analysis, we used Spearman correlations. Statistical analyses were performed with Statistica 13.3 (StatSoft Inc.).

3 | RESULTS

3.1 | Comparison of groups

Characteristics at inclusion are described in Table 1. Most AD patients (72%) took an acetylcholinesterase inhibitor. Caregiver was the spouse

RESEARCH IN CONTEXT

- 1. Systematic review:** Self-assessment of current capacities is used with a relative's evaluation to calculate a discrepancy score that reflects unawareness of impairment. Self-assessment as such was rarely considered in the literature to predict clinical evolution in participants with dementia.
- 2. Interpretation:** In a longitudinal evaluation, we found a positive relationship between both relative's and participant's evaluation of dependence in daily life activities at baseline and subsequent dependence of patients with Alzheimer's disease in activities adapted during a one-year cognitive rehabilitation program.
- 3. Future direction:** Self-assessment, relative's evaluation, and score of unawareness are variables of interest for subsequent evolution in clinical trials. An advance in patients' care would be to guide participants and their caregivers in realistic assessments of daily capacities to alleviate the consequences of the frequent and important clinical symptoms of unawareness.

in 79% of all participants. There was no difference in age and education but there were more men in the FTD group. Scores at the Neuropsychiatric Inventory (NPI-Q) showed slightly more severity and distress in the FTD group, but the difference between groups was not significant. The number of adapted activities varied between 3 and 12 in both groups (4.24 ± 1.31 in AD and 3.97 ± 1.12 in FTD), and did not significantly differ between groups from a qualitative and quantitative ($P = 0.29$) viewpoint.

At baseline (T1), global dependence in daily activities reported by the patient was similar in AD and FTD groups (Table 2). However, global dependence reported by the caregiver was significantly higher for FTD participants, and this was confirmed by a difference in caregiver minus patient discrepancy score ($P[\text{Mann-Whitney}] = 0.013$). Only one FTD participant had a negative discrepancy score while 23 AD participants (12%) had a negative score (indicating that participant reported more difficulties than the caregiver).

Neither global dependence reported by caregivers, nor the number of impaired activities among the 98 Profinteg IADLs, showed modification over time (Table 2). The delay between T1 and T2 was similar in both samples. However, the dependence for activities that were adapted by the therapists during the CR program was very significantly reduced after 1 year in both groups (with a large effect size, $\eta^2 = 0.30$, $P < 0.0001$). Decrease in dependence (more autonomy) was similar between groups ($26.90 \pm 27.67\%$ in AD and $25.63 \pm 25.98\%$ in FTD). Participants were compliant and they participated in all sessions proposed by the therapists.

At baseline, objective and subjective burden reported by the caregiver were similar in AD and FTD groups, as was the classical Zarit

TABLE 1 Characteristics at inclusion.

	AD	FTD	P (Mann-Whitney)
N	186	29	
Age	73.2 (7.8)	72.2 (8.5)	NS ($P = 0.54$)
Sex, F/M	93/93	8/21	Chi(1215) = 5.06; $P = 0.027$
Education, 1,2,3	39/60/87	8/8/13	NS ($P = 0.65$)
MMSE	23.5 (0.3)	23.8 (0.8)	NS ($P = 0.25$)
NPI-Q severity	5.9 (4.4)	7.6 (6.3)	NS ($P = 0.29$)
NPI-Q distress	8.1 (7.3)	10.6 (8.7)	NS ($P = 0.20$)

Note: Education: 1 = elementary school, 2 = lower secondary school; 3 = higher education.

Abbreviations: AD, Alzheimer's disease; FTD, frontotemporal dementia; F, female; M, male; MMSE, Mini-Mental State Examination; NPI-Q, Neuropsychiatric Inventory-Questionnaire; severity /36; distress /60; NS, not significant.

TABLE 2 Clinical characteristics.

	AD		FTD		ANOVA
	T1	T2	T1	T2	
Global dependence in IADL P %	12.58 (0.94)	N/A	13.94 (2.10)	N/A	
Global dependence in IADL C %	24.44 (1.28)	26.58 (1.69)	34.84 (3.26) ^b	37.71 (4.30) ^b	F(1213) = 7.71; $\eta^2 = 0.03$, $P = 0.006$
Discrepancy P/C %	11.86 (1.03)	N/A	20.90 (3.35) ^c	N/A	
Global dependence in adapted IADL C %	55.32 (1.66)	28.42 (1.95) ^a	59.73 (4.20)	34.12 (4.96) ^a	F(1213) = 91.85; $\eta^2 = 0.30$, $P < 0.0001$
Objective burden C %	8.17 (0.66)	6.41 (0.61) ^a	8.69 (1.68)	6.63 (1.54) ^a	F(1211) = 6.51; $\eta^2 = 0.03$, $P = 0.011$
Subjective burden C %	9.99 (0.74)	7.25 (0.71) ^a	14.19 (1.89)	9.18 (1.81) ^a	F(1209) = 21.15; $\eta^2 = 0.09$, $P < 0.0001$
Impaired activities	19.04 (0.73)	18.5 (0.92)	23.48 (1.87)	21.27 (2.32)	
ZARIT Max = 88	24.90 (0.99)	N/A	29.28 (2.75)	N/A	
Delay T1-T2 months	12.44 (0.08)	N/A	12.43 (0.20)	N/A	
MMSE	23.53 (0.29)	21.86 (0.37) ^a	23.83 (0.78)	23.62 (1.00)	F(1195) = 6.14; $\eta^2 = 0.03$, $P = 0.014$

Note: Mean and standard error are provided. η^2 = partial eta square. Adapted means daily activities adapted by the therapists during the cognitive rehabilitation program.

Abbreviations: AD, Alzheimer's disease; ANOVA, analysis of variance; C, caregiver; FTD, frontotemporal dementia; IADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination; P, participant; T1, baseline; T2, follow-up at 1 year; Zarit, Zarit Burden Interview.

^aDifference in time.

^bBetween groups difference.

^cP (Mann-Whitney). NS, non significant.

Burden Interview score. Importantly, both objective and subjective burden decreased over time, with a small ($\eta^2 = 0.03$, $P = 0.011$) and a medium effect size ($\eta^2 = 0.09$, $P < 0.0001$), respectively, in AD and in FTD groups.

MMSE score was similar between groups at T1, and it slightly decreased after 1 year in the AD participants.

3.2 | Regression and correlation analyses

In our AD patients included in a CR program, a multiple regression analysis tested the relationship between baseline global dependence for the 98 activities of the Profinteg tool and dependence for the adapted activities at 1 year, taking sex, age, education, and 1 year difference in MMSE score into account. When considering caregiver's

assessment, the global model was significant ($R^2 = 0.17$, $F[5, 162] = 8.00$, $P < 0.0001$), and global dependence at baseline reported by the caregiver ($b = 0.55$, $t[162] = 5.33$, $P < 0.0001$) and the difference in MMSE between T2 and T1 ($b = -1.07$, $t[162] = -2.12$, $P = 0.035$) were related to dependence for adapted activities at T2. Interestingly, when considering AD participant's assessment, the global model was also significant ($R^2 = 0.05$, $F[5, 162] = 2.81$, $P < 0.02$), and global dependence at baseline reported by the AD participants ($b = 0.30$, $t[162] = 2.00$, $P = 0.046$) and the difference in MMSE between T2 and T1 ($b = -1.24$, $t[162] = -2.27$, $P = 0.024$) were also related to (predictors of) dependence for adapted activities at T2. However, the significance was small (see scatter plots in Figure 1), and when both participant's and caregiver's assessment were entered in a model, the participant's assessment was not significant any more.

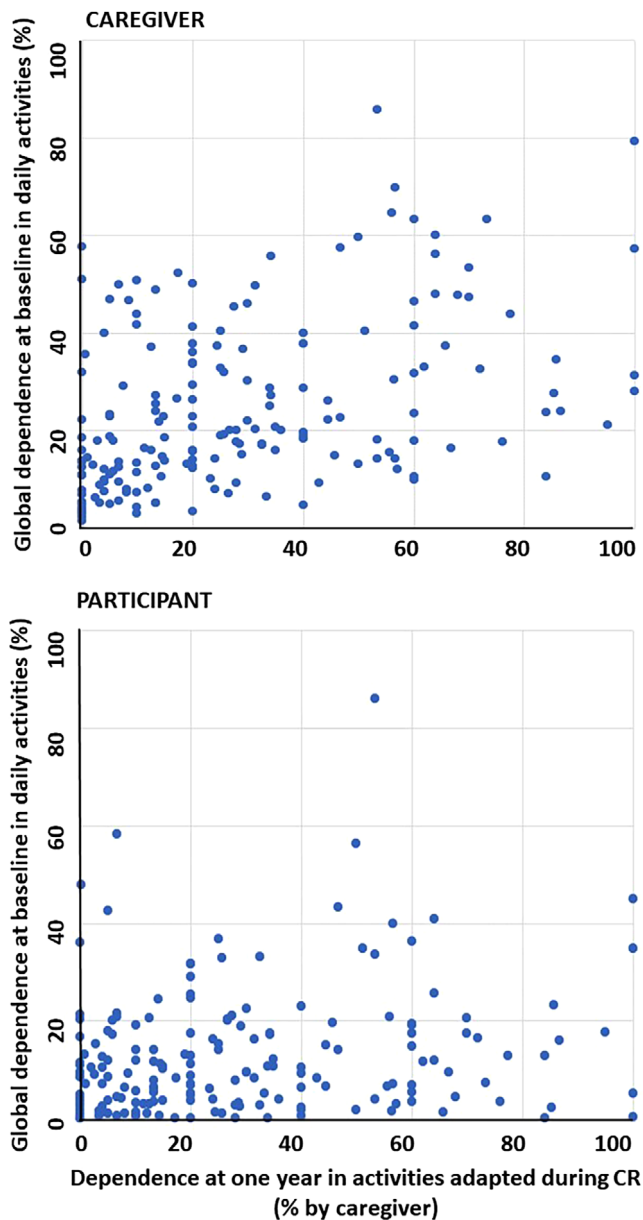


FIGURE 1 Scatter plots illustrating the relationship between dependence in activities adapted during the 1-year cognitive rehabilitation program and initial evaluation of global dependence in daily activities by the caregiver and the participant, respectively.

For sake of completeness, we considered also the discrepancy score (caregiver minus participant report). The global model was significant ($R^2 = 0.13$, $F[5, 162] = 6.10$, $P < 0.0001$), and discrepancy at baseline ($b = 0.57$, $t[162] = 4.42$, $P < 0.0001$) and the difference in MMSE between T2 and T1 ($b = -1.45$, $t[162] = -2.82$, $P = 0.005$) were predictors of dependence for adapted activities at T2. The greater the discrepancy score, the greater the dependence in activities adapted during the CR program.

In our smaller sample of FTD participants, baseline caregiver assessment of global dependence, but not participant assessment, was related to dependence for adapted activities at 1 year ($R = 0.54$, $t[27] = 3.27$, $P = 0.002$),

We finally observed that global dependence in IADL and objective burden were correlated at T2 in AD (Spearman $R = 0.49$, $P < 0.001$) and in FTD (Spearman $R = 0.63$, $P < 0.001$).

4 | DISCUSSION

We observed that unawareness for the level of dependence in daily activities measured by a discrepancy score was greater in bvFTD than in AD participants at baseline. This confirms the interest of unawareness as a clinical symptom in the diagnosis of FTD.^{4,14}

However, unawareness was only partial in our participants, because they accepted taking part in a cognitive rehabilitation program to adapt a few problematic activities of daily living. In our bvFTD participants, as in the AD group, there was a significant decrease in dependence (more autonomy) for activities that were adapted during the CR program. Moreover, burden of caregivers was decreased at 1 year compared to baseline assessment in both AD and FTD groups. There is a well established relationship between dependence and caregiver burden,^{20–22} and that is what we observed at follow-up in our samples, even in caregivers of FTD participants. Efficacy of cognitive rehabilitation programs for improving daily activities has been demonstrated in most randomized controlled trials in AD.^{23–26} Although we present a case series (without control group), the data show that FTD patients at an early stage may benefit from a CR program.

More importantly, in our AD sample, there was a significant relationship between a global assessment of dependence in IADL provided by both participants and caregivers at baseline and subsequent dependence in daily activities adapted by the therapists over 1 year. This observation means that even if participants were frequently less aware of their difficulties in daily life than their caregiver, their initial self-assessment was mildly predictive of their subsequent dependence in activities adapted during the CR program. This implies a careful interpretation of a discrepancy score.

Participants with subjective cognitive decline are aware of difficulties that cannot be observed with usual cognitive testing.²⁷ Awareness in MCI and early AD is always relative. This might depend on the measurement used,²⁸ but also on the domain considered.²⁹ For example, patients may lack awareness for memory impairment but recognize language difficulties.⁴ More positive self-rating of functional abilities was shown to be related to more education, less depression, and better performance in episodic memory (recall) and naming in early-stage dementia.¹⁰ In a community sample, memory complaints were associated with poor cognitive performances.³⁰ Participant judgment was rarely considered as such to assess awareness in AD.^{9–11,31} Interestingly, concerns about forgetfulness (anosodiaphoria) was not predictive of evolution to AD in MCI participants.³

When one considers dependence in daily activities, a cross-sectional relationship has been reported between greater dependence and unawareness for cognitive impairment measured with a discrepancy score.^{32,33} In a previous prospective study with few AD participants, higher levels of awareness for memory difficulties using a discrepancy

score were related to better learning of face–name associations after cognitive intervention.³⁴ However, in a preliminary investigation of a few weeks of a memory and coping intervention program in a small sample of patients with mild to moderate dementia, caregiver's evaluation of improvement in the everyday memory functioning (compared to a control group) was not related to baseline anosognosia rated by a therapist.⁶ In a recent cross-sectional analysis of baseline data obtained in a large population included in a longitudinal research program (IDEAL), better patient awareness concerning dependence in daily living activities (measured with a discrepancy score) was related to the fact that patients with dementia had better memory and received less than 1 hour of care per day from the informant.³⁵ As expected, our study in a relatively large sample of patients shows that better awareness of daily difficulties at inclusion is related to lower dependence in daily activities 1 year after involvement in a CR program. This is in keeping with studies reporting that unawareness of cognitive impairment is predictive of subsequent decline in MCI.^{2,3,36} Moreover, in our longitudinal study, the decrease in cognitive performance, measured by a 1 year minus baseline difference in MMSE scores, was related to the informant assessment of dependence in daily activities at 1 year. The relationship between cognition and IADL is well established.^{37,38} In a previous cross-sectional study for example, less positive informant rating of functional ability was associated with lower MMSE score in patients with different types of dementia.¹⁰

A limitation of the study is the use of a questionnaire for the assessment of the level of dependence (for which participant and caregiver provide subjective judgment) rather than direct observation (which was part of the rehabilitation procedure). Another is the lack of longitudinal data from a non-intervention group of participants that would have allowed us to test whether the association between participant and caregiver assessment at baseline and 1 year dependence in daily activities is specifically related to the result of the CR program. The importance of baseline awareness of daily dependence for subsequent autonomy does not diminish the interest of other variables such as performance in different cognitive domains, behavioral and psychological symptoms, lifestyle, and medical risk factors that are taken into account in other studies of ageing populations.

In conclusion, the data obtained in a large population of participants with neurodegenerative dementia emphasize the interest to consider not only caregivers but also (to a lesser extent) participant assessment of IADL for understanding the evolution of dependence in daily life. An advance in patients' care would be to guide participants and their caregivers in realistic assessments of daily capacities to alleviate the consequences of the frequent and important clinical symptoms of unawareness.

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CONFLICT OF INTEREST STATEMENT

The authors do not have any conflicts of interest. Author disclosures are available in the [supporting information](#).

CONSENT STATEMENT

Written informed consent to participate was obtained from the patient and the relative.

ORCID

Eric Salmon  <https://orcid.org/0000-0003-2520-9241>

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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