Apathy Among Institutionalized Stroke Patients: Prevalence and Clinical Correlates

Suzanne van Almenkerk, M.A., Martin Smalbrugge, M.D., Ph.D., Marja F.I.A. Depla, Ph.D., Jan A. Eefsting, M.D., Ph.D., Cees M.P.M. Hertogh, M.D., Ph.D.

Objectives: *Apathy is a frequent neuropsychiatric consequence of stroke. In the underresearched population of institutionalized stroke patients, we aimed to explore the prevalence of apathy, its clinical correlates, and the relation to the amount of stimulating activities in the nursing home (NH).* **Design:** *A cross-sectional, observational study.* **Setting:** *Dutch NHs.* **Participants:** *274 chronic stroke patients.* **Measurements:** *Data were collected through observation lists that were filled out in structured interviews with qualified nurse assistants who knew the residents well. The lists comprised the NH-version of the Apathy Evaluation Scale (AES10), the Barthel Index, the Neuropsychiatric Inventory Questionnaire, and sections of the Resident Assessment Instrument for Long-Term Care Facilities. Attending physicians and therapists provided additional information.* **Results:** *Apathy (AES10 score ≥30) was present in 28% of residents. Multilevel regression analyses revealed that this apathy was independently related to (moderate, severe) cognitive impairment (odds ratio [OR] 11.30 [95% confidence interval (CI): 4.96−25.74], OR 5.54 [95% CI: 2.48−12.40]), very severe ADL-dependency (OR 12.10 [95% CI: 1.35−108.66]), and being >12 hours per day in bed (OR 2.10 [95% CI: 1.07−4.13]). It was not related to depressive mood symptoms (OR 1.75 [95% CI: 0.91−3.37]). Only in residents aged less than 80 years were a higher amount of activities independently related to a lower AES10 score (−0.70 [95% CI: −1.18 to −0.20] points per four extra activities in a 4-week period).* **Conclusions:** *Apathy is prevalent in largely one-quarter of institutionalized stroke patients, and that is most strongly related to cognitive impairment in this explorative study. We discuss the need for research on the relation with distinct dimensions of depression and fatigue as partly overlapping constructs, and on (individualized) stimulating activities as a possible intervention method.* (Am J Geriatr Psychiatry 2015; 23:180−188)

Key Words: Apathy, stroke, long-term care, neuropsychiatry

The interest in the wide variety of neuropsychiatric consequences of stroke is growing worldwide.[1] This neuropsychiatric spectrum includes the syndrome of apathy, defined as a persisting disorder of motivation that can be manifested in reduced goal-directed behavior, reduced goal-directed cognition, and reduced emotions.[2,3] Two recent meta-analyses found a pooled rate of post-stroke apathy

Received September 18, 2013; revised March 25, 2014; accepted March 26, 2014. From the VU University Medical Center, Department of General Practice and Elderly Care Medicine and EMGO Institute for Health and Care Research, Amsterdam, The Netherlands. Send correspondence and reprint requests to Suzanne van Almenkerk, M.A., VUmc, BS7, Room-B543, 1081 BT-Amsterdam, The Netherlands. e-mail: s.vanalmenkerk@vumc.nl

http://dx.doi.org/10.1016/j.jagp.2014.03.011

of 35%–36%.[4,5] It seems to be rather stable over time, as shown by longitudinal studies with a follow-up of 6–15 months post-stroke.[6–8]

In this study we focus on the under-researched population of chronic stroke patients who are dependent on institutional long-term care. From several perspectives we may expect this group of stroke survivors to be highly prone to apathy. Firstly, apathy can arise as a direct consequence of brain damage, which is most severe in this population. Neuroimaging and pharmacological studies on apathy in various patient populations indicate the involvement of frontal lobes and connected subcortical structures.[9,10] Secondly, post-stroke apathy is shown to be consistently associated with depression, higher rates of cognitive impairment, and increased disability.[4,5] These impairments are all highly prevalent in our study population.[11] Finally, apathy may occur as a normal human response to the environment of the nursing home (NH) in which the usual resources of stimulation are removed. Some evidence exists that an increase of stimulation, such as cognitive stimulation activities,[12] individual activity therapy,[13] and multi-sensory stimulation,[14] might reduce apathy in NH residents with dementia.

Results of longitudinal studies on post-stroke apathy indicate negative effects on physical and cognitive recovery,[15,16] social participation, and health perception.[7] In a large cohort of NH residents with and without dementia, apathy appeared as the most significant risk factor for weight loss.[17] These adverse outcomes highlight the need for a better recognition and understanding of post-stroke apathy in the NH, and for exploring possible intervention strategies that might enhance quality of life. As part of our aim to develop an integrated care and treatment program for institutionalized stroke patients, we aim to explore the following research questions: 1) What is the prevalence of apathy among institutionalized stroke patients? 2) What are the clinical correlates of this apathy? 3) Is the amount of stimulating activities in the NH in which a resident participates, related to the severity of apathetic behavior?

METHODS

This study is part of the CAre for STroke In LOng term care facilities in the Netherlands (CASTILON) study. From May 2008 to July 2009 a cross-sectional, observational study design was used to collect data of chronic stroke patients who received long-term care in 17 Dutch NHs.[11] Attending physicians (in Dutch NHs delivered by specifically trained physicians, referred to as elderly care physicians [ECPs]) were asked to select their patients according to the following inclusion criteria: 1) stroke was the main diagnosis for NH admission, 2) the last stroke occurred 3 months or more ago, 3) the need for long-term care was indicated by the multidisciplinary stroke team and discussed with the stroke patient and their relatives, and 4) the resident stayed 1 month or more on a somatic long-term care ward. We collected data on each resident through an observation list that was filled out in a structured interview with a qualified nurse assistant who knew the resident well. All nurse assistants were interviewed by the same trained research assistant. As we will describe subsequently, additional information was provided by the attending ECP and therapists. A total of 284 residents were included (ranging from 3–31 residents per NH), of which 10 cases were excluded because of incomplete questionnaires. The study protocol was approved by the medical ethics committee of the VU University Medical Center.

Measurements

Apathy. Apathetic behavior was measured with a NH-version of the Apathy Evaluation Scale (AES10).[18] This AES10 strongly correlates to the original 18-item AES that is one of the most psychometrically robust measures for assessing apathy.[19] It consists of ten items, each giving an example of apathetic behavior. Each item is evaluated on a four-point scale, ranging from 1 (not at all characteristic) to 4 (very characteristic), based on observations of the resident's behavior in the last month.

Severity of apathetic behavior. The AES10 score (sum of all item scores) represents the severity of apathetic behavior, ranging from 10 (no apathetic behavior) to 40 (maximum apathetic behavior).

Apathy. We considered an AES10 score of 30 or higher as indicative for apathy. In a first and preliminary validation study against the first and only formal diagnostic criteria for apathy to date,[2] this cut-off score had the highest sum of sensitivity (0.71) and specificity (0.70) in a heterogeneous NH population.[20]

Clinical covariates.

Demographics. We administered age, sex, marital status, and educational level.

Stroke characteristics. ECPs provided information about stroke subtype (hemorrhagic or ischemic), stroke location (left-sided or right-sided, the category 'other location' not included in the analyses), and time post-stroke.

Comorbidity. ECPs provided information about the presence of diagnoses other than stroke that influenced a resident's current status of functioning or for which active treatment was given. We counted the total number of different diagnoses according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision coding system, and dichotomized it on the median.

Dependency in basic activities of daily living (ADL). ADL dependency was measured by the 20-point Barthel Index (BI), categorized as *very severe* (BI 0−4),[21] *severe* (BI 5−11), and *moderate/mild* (BI ≥12).[22]

Pain. We assessed pain frequency and intensity through the corresponding items of the Dutch version of the Minimum Data Set of the Resident Assessment Instrument for Long-Term Care Facilities (RAI-LTCF).[23] Pain frequency is coded as no pain (0), less than daily pain (1), and daily pain (2) in the last 7 days; pain intensity is coded as no pain, mild pain (0), moderate pain (1), and severe pain (2, defined as "times when pain is horrible or excruciating") in the last 7 days. We defined pain as substantial when the product of pain frequency and pain intensity was greater than or equal to 2,[24] referring to severe, or daily moderate pain.

Fatigue or bedrest. To the best of our knowledge there is no valid observation instrument to measure fatigue. Based on a "case definition" of post-stroke fatigue ("the patient experiences a persistent lack of energy, or an increased need to rest every day or nearly every day, leading to difficulty taking part in everyday activities"),[25] we asked the nurse assistant how many hours in a 24-hour day the resident stayed in bed, and dichotomized this on the median.

Cognitive functioning. We assessed cognitive functioning through the RAI-LTCF Cognitive Performance Scale (CPS), which has good agreement with the Mini Mental State Examination in the detection of cognitive impairment in NH residents.[26] The CPS is a seven-category index, ranging from cognitively intact (0) to very severely impaired (6). We categorized the CPS by combining the three severe categories as *severe* (CPS 4−6), the middle two categories as *moderate* (CPS 2−3), and the remaining two categories as *no/mild* cognitive impairment (CPS 0−1).

Emotional functioning. We assessed a broad range of neuropsychiatric (NP) symptoms using the Neuropsychiatric Inventory Questionnaire (NPIQ).[27] Each domain is assessed by a screening question that covers core symptom manifestations. When these symptoms are present in the last month, symptom severity is evaluated on a three-point scale (1-mild, 2-moderate, 3-severe).

(i) Clinically relevant depressive symptoms: We analyzed the NPIQ-item dysphoria/depression as an individual NP symptom, and defined it to be clinically relevant when its severity was moderate or severe (i.e., score ≥2).

(ii) Modified NPIQ-score: The sum of all item scores, except the items apathy/indifference (already assessed through the AES10) and dysphoria/depression (analyzed as an individual NP symptom). The modified score represents the amount of emotional distress in the domains of delusions, hallucinations, agitation/aggression, anxiety, elation/euphoria, disinhibition, irritability/lability, aberrant motor behaviors, night-time behavioral disturbances, and appetite/eating disturbances, and ranges from 0 (no NP symptoms present) to 30 (all remaining NP symptoms present with maximum severity).

Communicative functioning. We assessed expression through the RAI-LTCF item ability to make him/herself clear,[28] which is evaluated on a five-point frequency scale (always, usually, often, sometimes, and rarely or never). We dichotomized the score by combining the first three categories in good/moderate and the last two categories in poor.

Psychotropic drugs. The researchers MS, JE, and CH reviewed medication lists to identify the use of psychotropics in the following categories: antipsychotics (AP), antidepressants (AD), anxiolytics/hypnotics (Anx/Hyp), antiepileptics (AE), and other psychotropics (OP). Additionally, we counted for each resident the total number of categories.

Stimulating activities. We defined a stimulating activity as any therapeutical or social activity that was offered by a NH professional outside routine daily care, and in which the resident participated.

TABLE 1. Characteristics of Institutionalized Stroke Patients With and Without Apathy and Multilevel Bivariate Regression Analyses with Apathy as Outcome Measure

	Apathy (N = 77) N (%)	No Apathy (N = 197) N (%)		95% CI	
			crude OR	lower	upper
Age ≥80 years	38 (49.4)	82 (41.6)	1.51	0.87	2.62***
Female sex	44 (57.1)	116 (58.9)	0.98	0.57	1.69
Single/widowed	49 (63.6)	120 (60.9)	1.20	0.69	2.09
Education *(no. missing = 102)*					
only primary	17 (34.7)	48 (39.0)	1.05	0.37	2.96
secondary	25 (51.0)	55 (44.7)	1.35	0.50	3.69
high	7 (14.3)	20 (16.3)	reference		
Ischemic stroke *(no. missing = 12)*	63 (85.1)	150 (79.8)	1.60	0.75	3.41
Right-sided stroke *(no. missing = 29)*	34 (48.6)	98 (56.0)	0.76	0.43	1.34
Time post-stroke (years)					
≤2	18 (23.4)	54 (27.4)	reference		
2 ≤ 4	20 (26.0)	48 (24.4)	1.27	0.59	2.74
4 ≤ 7	25 (32.5)	43 (21.8)	1.80	0.85	3.80***
>7	14 (18.2)	52 (26.4)	0.74	0.33	1.68
≥2 comorbid diagnoses	42 (54.5)	105 (53.3)	1.06	0.62	1.81
Dependency in basic ADL					
moderate/mild (BI ≥12)	1 (1.3)	24 (12.2)	reference		
severe (BI 5–11)	20 (26.0)	97 (49.2)	4.78	0.58	39.60***
very severe (BI 0–4)	56 (72.7)	76 (38.6)	18.32	2.27	147.73*
Substantial pain	24 (31.2)	52 (26.4)	1.16	0.64	2.10
Bedrest >12 hr per day	51 (66.2)	88 (44.7)	2.50	1.41	4.40*
Cognitive impairment					
no/mild (CPS 0–1)	15 (19.5)	129 (65.5)	reference		
moderate (CPS 2–3)	24 (31.2)	43 (21.8)	5.34	2.48	11.52*
severe (CPS 4–6)	38 (49.4)	25 (12.7)	15.67	7.28	33.73*
Clinically relevant depressive symptoms	37 (48.1)	70 (35.5)	1.68	0.96	2.85**
Modified NPIQ-score (mean ± SD [range])	5.00 ± 4.25 [0–20]	4.28 ± 4.17 [0–19]	1.03	0.97	1.10
Poor expression	38 (49.4)	38 (19.3)	4.31	2.40	7.74*
Psychotropics					
Antipsychotics	9 (11.7)	13 (6.6)	1.66	0.67	4.14
Antidepressants	32 (41.6)	69 (35.0)	1.26	0.73	2.19
Anxiolytics/Hypnotics	22 (28.6)	64 (32.5)	0.80	0.44	1.45
Antiepileptics	14 (18.2)	44 (22.3)	0.71	0.36	1.41
Other	1 (1.3)	3 (1.5)	0.88	0.09	8.85
No. of categories (mean ± SD [range])	1.01 ± 0.94 [0–3]	0.98 ± 0.87 [0–3]	0.98	0.72	1.34

Notes: ADL: activities of daily living; BI: Barthel Index; CPS: Cognitive Performance Scale; modified NPIQ-score: Neuropsychiatric Inventory Questionnaire score except the items dysphoria/depression and apathy/indifference; SD: standard deviation; OR: odds ratio; CI: confidence interval. p-values are based on a Wald χ^2 test with df = 1. *p <0.01, **p <0.10, ***p <0.20.

All attending paramedical therapists (physical therapist, occupational therapist, speech/language therapist, dietician), psychosocial therapists (psychologist, social worker, spiritual carer), and activity therapists provided information about the amount of individual and group activities in which the resident participated. We counted the total amount of activities in the last 4 weeks that lasted more than 15 minutes.

Statistical Analyses

We generated descriptive statistics for all assessed variables using IBM SPSS Statistics version 20.

To investigate the clinical correlates of apathy, we performed multilevel logistic regression techniques with AES10 score 30 and higher as the outcome measure. Firstly, we conducted bivariate regression analyses, resulting in crude odds ratios (ORs) and 95% confidence intervals (CIs). Assumptions of linearity were checked for all continuous measures, but were not confirmed for age and time post-stroke. As a consequence, we transformed these variables into categories. Subsequently, we selected the variables that were associated with apathy at the p <0.20 level, entered these into the multivariate model, and checked for collinearity. We used a backward selection

procedure based on the Wald statistic, until all clinical covariates were associated with apathy at the $p < 0.10$ level. The level of significance was set at $p < 0.05$.

To investigate the relation between the amount of stimulating activities and the severity of apathetic behavior, we performed multilevel linear regression techniques with the AES10 score as outcome measure. We investigated whether age and sex modified the relation, by adding each interaction term separately to the bivariate model (significance level $p < 0.10$). Then all assessed clinical covariates were entered into the model as possible confounders. Assumptions of linearity and normality of the final model were checked with an analysis of residuals.

We used multilevel analyses to adjust for possible dependency of observations, due to the clustering of individual residents (first level) within ECPs (second level) and NHs (third level).[29] These analyses were performed with second-order penalized quasi-likelihood estimation procedures, using MLwiN 2.24 (Centre for Multilevel Modeling, University of Bristol, UK).

RESULTS

Prevalence of Apathy

In the total study sample of 274 residents (mean age 76.6 years, 58.4% women, median time post-stroke 47 months), the mean AES10 score was 23.73 (±9.10, range: 10–40). Apathy (defined as AES10 score ≥30) was prevalent in 28.1% of the residents (N = 77). Across the NHs, the mean AES10 score ranged from 19.67 ± 4.93 to 31.32 ± 7.91, and the apathy rate from 0% (N = 0 out of 3) to 59.1% (N = 13 out of 22).

Clinical Correlates Of Apathy

Table 1 describes the characteristics of the residents with and without apathy, together with the results of the multilevel bivariate regression analyses on apathy (crude ORs). In these analyses apathy appeared to be associated with more dependency in basic ADL, being more than 12 hours per day in bed, more cognitive impairment, and poor expression, all at the $p < 0.01$ level. All clinical covariates associated with apathy at the $p < 0.20$ level were selected for the multilevel multivariate regression analysis. Table 2 shows the final result after the backward selection procedure. Based on evaluation of the Wald values, apathy showed the strongest association with cognitive impairment (OR 11.30 [95% CI: 4.96–25.74] for severe, and OR 5.54 [95% CI: 2.48–12.40] for moderate cognitive impairment). Very severe ADL-dependency (OR 12.10 [95% CI: 1.35–108.66], referenced to the category moderate/mild), and being more than 12 hours per day in bed (OR 2.10 [95% CI: 1.07–4.13]) appeared as the other clinical correlates of apathy. The presence of clinically relevant depressive symptoms was not significantly associated with apathy (OR 1.75 [95% CI: 0.91–3.37], $p = 0.096$).

TABLE 2. Clinical Correlates of Apathy Among Institutionalized Stroke Patients: Multilevel Multivariate Regression Analysis

		95% CI		
	adj OR	Lower	Upper	Wald χ^2
Dependency in basic ADL				
Moderate/mild (BI ≥12)	reference			
Severe (BI 5–11)	5.50	0.60	50.69	2.27
Very severe (BI 0–4)	12.10	1.35	108.66	4.96**
Bedrest >12 hr per day	2.10	1.07	4.13	4.67**
Cognitive impairment				
No/mild (CPS 0–1)	reference			
Moderate (CPS 2–3)	5.54	2.48	12.40	17.35*
Severe (CPS 4–6)	11.30	4.96	25.74	33.34*
Clinically relevant depressive symptoms	1.75	0.91	3.37	2.77

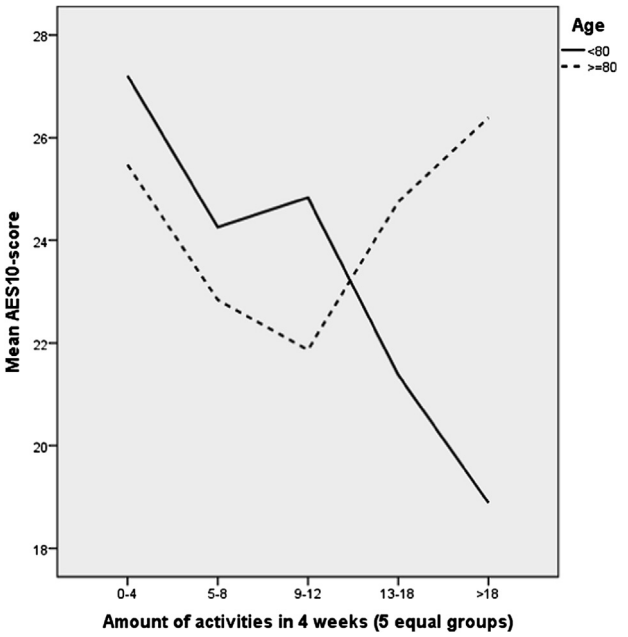
Notes: ADL: activities of daily living; BI: Barthel Index; CPS: Cognitive Performance Scale; SD: standard deviation; adj OR: adjusted odds ratio; CI: confidence interval. This table shows the final result of the multilevel multivariate regression analysis of preselected variables ($p < 0.20$ level in the multilevel bivariate regression analyses, see Table 1) after backward selection. p-values are based on a Wald χ^2 test with df = 1. *$p < 0.01$, **$p < 0.05$.

Relation between Apathetic Behavior and Amount of Stimulating Activities

In the total study sample, residents participated in a median amount of 10 (interquartile range [IQR]: 5–17, range: 0–72) activities in a 4-week period. The association between the amount of activities and the AES10 score appeared to be modified by age (Wald $\chi^2 = 6.95$, df = 1, $p < 0.01$). Because of this interaction effect, we present the results for both age groups separately.

Residents aged less than 80 years and 80 years and older participated in a median amount of 11 (IQR: 5−18, range: 0−72) respectively 8 (IQR: 4−15, range: 0−46) activities (Mann-Whitney U-test, z = −2.48, p = 0.01). The relation between the amount of activities and the AES score for both age groups is illustrated in Figure 1. Table 3 shows the stratified results of the multilevel regression analyses. Only in the younger residents did the association appear to be significant: four extra activities in a 4-week period were associated with a lower AES10 score of −0.94 (95% CI: −1.38 to −0.50) points in the crude model. This association sustained when the model was corrected for all assessed clinical covariates (−0.70 [95% CI: −1.18 to −0.20] points).

FIGURE 1. Relation between the amount of stimulating activities in a 4-week period (in five equal groups) and the severity of apathetic behavior (measured through the Apathy Evaluation Scale - nursing home version) for residents aged less than 80 years and 80 years and older.



DISCUSSION

This explorative, cross-sectional study among institutionalized stroke patients indicates that apathy is prevalent in 28% of residents. This apathy is most strongly associated with cognitive impairment, but not related to clinically relevant depressive symptoms. Other clinical correlates are very severe ADL dependency and being in bed more than 12 hours per day. Finally, the results suggest that the greater number of activities in which a resident participates is related to less severe apathetic behavior. This association is of small size, however, and appears only in residents less than 80 years.

A major strength of this study is the uniqueness of the study sample, representing an under-researched population on the continuum of stroke care. The use of observation instruments enabled us to include all residents, even those with severe cognitive and/or communicative impairments. A second strength is that we classified apathy through an assessment instrument that is not only psychometrically robust, but also for the first time (preliminarily) validated against the first and only diagnostic criteria for apathy to date, in contrast to most previous studies on apathy.[10] However, the observed sensitivity and specificity of the optimal cutoff score (AES10 ≥30) still represent a certain misclassification of the presence or absence of apathy. Much more validation research has to be done in the NH and stroke population, both on the diagnostic criteria as gold standard and on assessment instruments. Our study is mainly limited by its cross-sectional design, which does not allow us to gain insight in the evolution of symptoms and the direction of causal pathways. Nevertheless, the results provide good insight in the manifestation of apathy in everyday clinical practice, in relation to what is already known from the literature. This should encourage NH professionals to further examine the presence of post-stroke apathy and to explore interventions that may enhance quality of life.

TABLE 3. Multilevel Linear Regression Analyses of the Association Between the Amount of Stimulating Activities and Severity of Apathetic Behavior (AES10 Score)

Per increase of 4 activities in 4 weeks		95% CI			95% CI	
	Crude β	Lower	Upper	Adj β	Lower	Upper
Age <80 years	−0.94	−1.38	−0.50*	−0.70	−1.18	−0.20*
Age ≥80 years	0.13	−0.54	0.81	0.22	−0.47	0.91

Notes: β indicates the difference in AES10-score; adj: adjusted for all assessed clinical covariates. *p <0.05. p-values are based on a Wald χ^2 test with df = 1.

We found a lower prevalence of post-stroke apathy than the pooled rate of 35%–36% in the recent meta-analyses.[4,5] Van Dalen et al. additionally performed a sensitivity analysis of studies using the recommended AES and/or the apathy subscale of the NPI,[19] which resulted in an estimated apathy prevalence of 26.3% (20.5%–33.1%), similar to our result of 28%. The meta-analysis, though, also showed a substantial and persistent heterogeneity, making a comparison of results difficult. Given the long time post-stroke in our study population (median: 47 months), longitudinal research on apathy using validated apathy measures is very desirable. As mentioned in the Introduction, existing longitudinal studies seem to indicate that apathy is rather stable over time.[6–8] Recently, however, Mikami et al.[15] showed that apathy in the first year post-stroke lasted on average almost 6 months. Their study population, however, was small and very selective (56 patients who received placebo as part of a larger treatment trial).

In accordance with the literature, cognitive impairment appeared as a strong clinical correlate of apathy. Firstly, it is likely that loss of cognitive capacities limits a person's ability to organize goal-directed behavior.[30] In this view, apathy appears as an intrinsic symptom (or marker) of cognitive deterioration rather than a distinct neuropsychiatric syndrome. This might be true for a subgroup of apathetic residents in our study. Secondly, both apathy and cognitive impairment might be caused by the same underlying brain damage. The frontal lobes and connected subcortical structures that are thought to be involved in apathy are also related to various cognitive functions.[5] It seems relevant to investigate in future research the relation between apathy and distinct cognitive functions. For example, a study among ischemic stroke patients showed that apathy was associated with reduced attention and speed of information processing.[31]

In contrast to what we expected from the recent reviews, we were not able to demonstrate an independent relationship between apathy and (moderate or severe) depressive symptoms. As Hama et al.[32] argued, the current concept of post-stroke depression incorporates both an affective (depressed mood) and an apathetic (loss of interest) dimension. As shown by previous stroke studies, apathy can then be expected to be associated as partly overlapping construct. In contrast, the NPIQ-item dysphoria/depression only addresses a depressed mood that appeared not to be related to apathy in our study. The importance of the distinction between isolated post-stroke apathy and apathy in the context of post-stroke depression is consistently underlined in the literature, mainly because both conditions lead to different treatment options.[2,5,9] When apathy is misdiagnosed as depression and treated by selective serotonine reuptake inhibitors, this may even induce apathy.[33] To increase our understanding of the relation between both constructs, our result supports the notion that future research should focus on the distinct dimensions of depression, rather than on the formal, multidimensional diagnosis. A careful selection of rating scales could make this possible.[9] Also research on the relation with stroke location would be very valuable. Recent brain imaging findings suggest that affective and apathetic symptoms after stroke are associated with different neuroanatomic pathways.[34]

The demonstrated relation between apathy and dependency in basic ADL is in line with previous findings.[5] Severe dependency may cause apathetic behavior, either as an emotional response[32] or because the dependency limits a person's ability to respond to the environment.[30] Reversely, some evidence exists that apathy can lead to less recovery in ADLs.[15,16] Finally, we would like to focus on a possible underlying factor causing both apathy and ADL dependency. In the context of the third clinical correlate we found (being in bed >12 hours per day), we hypothesize that fatigue might be this underlying factor. With respect to ADL dependency, fatigue was identified as an independent predictor in a large cohort study.[35] We will now further discuss the relation between fatigue and apathy.

Although we have to be very cautious to interpret the amount of bedrest as an indicator for fatigue, we may at least assume that fatigue is a considerable problem in our study population of survivors of the most severe strokes. From the literature we know that post-stroke fatigue is prevalent in 35%–92% of patients in the first 6 months post-stroke, likely to persist in the long term for patients who develop it,[36] and is an independent predictor for institutionalization after stroke.[35] Moreover, evidence exists that apathetic behavior can be an expression of experienced fatigue. In the development of a

self-report instrument, Smets et al.[37] identified reduced motivation and reduced activity as relevant dimensions of fatigue (besides general, physical, and mental fatigue). To the best of our knowledge, the relation between apathy and fatigue has not been studied in stroke patients to date. Again, to improve our understanding of the relation between both constructs, our results suggest that future research should focus on the distinct dimensions of fatigue, rather than on a general definition of fatigue.

With respect to our last research question, we found that a higher amount of stimulating activities was independently related to less apathetic behavior in residents less than 80 years, suggesting that an increase of stimulation might reduce apathetic behavior. Of course, our cross-sectional design cannot reveal such a causal relationship, and only future experimental research could verify this hypothesis and evaluate its clinical relevancy. Then, it will be important to use a broader definition of stimulating activities, including activities that are offered by informal caregivers and/or relatives. Although we were not able to demonstrate an independent relationship in the high-aged group, the results showed that these residents participated in significantly fewer activities than the younger residents. Therefore, the absence of the association could be explained by loss of statistical power, implicating that high-aged residents should not be excluded beforehand from future research. It might even be—as the Figure 1 suggests—that there is an optimum number of stimulating activities to reduce apathetic behavior in residents aged 80 years and older, beyond which an adverse effect arises. It is imaginable that too many stimulating activities could lead to an increase of apathetic behavior (e.g., due to mental fatigue or resistance), and that this point is reached sooner in the high-aged. Finally, the most interesting question to answer with respect to this topic is which elements of stimulating activities are crucial for (possibly) reducing apathy. Are these general aspects such as time and attention (in some small intervention trials among dementia patients used as control elements[12,13]), and/or the specific nature of an activity? For example, previous research showed that introducing a nursing guideline that focused on increasing individualized pleasant activities reduced depression in NH residents with dementia,[38] and possibly in institutionalized stroke patients.[39] We would recommend that future research investigates the efficacy of such intervention methods on both depression and apathy. This might be combined with pharmacological interventions that showed promising results.[40]

In conclusion, this explorative study shows that apathy is prevalent in largely one-quarter of institutionalized stroke patients. It is most strongly related to cognitive impairment, but not to depressive mood symptoms. Further research on apathy in relation to distinct dimensions of depression and fatigue would improve our understanding of the possible overlap with these multidimensional constructs. The demonstrated relation between a greater number of stimulating activities and less severe apathetic behavior encourages future experimental research on this possible intervention method.

Funding was provided by Zonnehuisgroep Vlaardingen, Vereniging het Zonnehuis, and De Open Ankh (Dutch health care organizations), and the University Network of Organizations for Care for the Elderly of the VU University Medical Center (UNO-VUmc, Netherlands).

We thank all the residents and personnel of the NHs who made this study possible, and our research assistant Anneke van Paridon for her help with the data collection. There are no disclosures to report.

References

1. Robinson RG: Evolving research in the geriatric neuropsychiatry of stroke. Am J Geriatr Psychiatry 2013; 21:817–820
2. Robert P, Onyike CU, Leentjens AF, et al: Proposed diagnostic criteria for apathy in Alzheimer's disease and other neuropsychiatric disorders. Eur Psychiatry 2009; 24:98–104
3. Starkstein SE, Leentjens AF: The nosological position of apathy in clinical practice. J Neurol Neurosurg Psychiatry 2008; 79: 1088–1092
4. Caeiro L, Ferro JM, Costa J: Apathy secondary to stroke: a systematic review and meta-analysis. Cerebrovasc Dis 2013; 35:23–39
5. van Dalen JW, Moll van Charante EP, Nederkoorn PJ, et al: Poststroke apathy. Stroke 2013; 44:851–860
6. Castellanos-Pinedo F, Hernandez-Perez JM, Zurdo M, et al: Influence of premorbid psychopathology and lesion location on affective and behavioral disorders after ischemic stroke. J Neuropsychiatry Clin Neurosci 2011; 23:340–347

7. Mayo NE, Fellows LK, Scott SC, et al: A longitudinal view of apathy and its impact after stroke. Stroke 2009; 40:3299–3307
8. Withall A, Brodaty H, Altendorf A, et al: A longitudinal study examining the independence of apathy and depression after stroke: the Sydney Stroke Study. Int Psychogeriatr 2011; 23:264–273
9. Ishii S, Weintraub N, Mervis JR: Apathy: a common psychiatric syndrome in the elderly. J Am Med Dir Assoc 2009; 10:381–393
10. van Reekum R, Stuss DT, Ostrander L: Apathy: why care? J Neuropsychiatry Clin Neurosci 2005; 17:7–19
11. van Almenkerk S, Depla MFIA, Smalbrugge M, et al: Institutionalized stroke patients: status of functioning of an under researched population. J Am Med Dir Assoc 2012; 13:634–639
12. Niu YX, Tan JP, Guan JQ, et al: Cognitive stimulation therapy in the treatment of neuropsychiatric symptoms in Alzheimer's disease: a randomized controlled trial. Clin Rehabil 2010; 24:1102–1111
13. Politis AM, Vozzella S, Mayer LS, et al: A randomized, controlled, clinical trial of activity therapy for apathy in patients with dementia residing in long-term care. Int J Geriatr Psychiatry 2004; 19:1087–1094
14. Verkaik R, van Weert JC, Francke AL: The effects of psychosocial methods on depressed, aggressive and apathetic behaviors of people with dementia: a systematic review. Int J Geriatr Psychiatry 2005; 20:301–314
15. Mikami K, Jorge RE, Moser DJ, et al: Incident apathy during the first year after stroke and its effect on physical and cognitive recovery. Am J Geriatr Psychiatry 2013; 21:848–854
16. Santa N, Sugimori H, Kusuda K, et al: Apathy and functional recovery following first-ever stroke. Int J Rehabil Res 2008; 31: 321–326
17. Volicer L, Frijters DH, van der Steen JT: Apathy and weight loss in nursing home residents: longitudinal study. J Am Med Dir Assoc 2013; 14:417–420
18. Lueken U, Seidl U, Volker L, et al: Development of a short version of the Apathy Evaluation Scale specifically adapted for demented nursing home residents. Am J Geriatr Psychiatry 2007; 15:376–385
19. Clarke DE, Ko JY, Kuhl EA, et al: Are the available apathy measures reliable and valid? A review of the psychometric evidence. J Psychosom Res 2011; 70:73–97
20. Leontjevas R, Evers-Stephan A, Smalbrugge M, et al: A comparative validation of the Abbreviated Apathy Evaluation Scale (AES-10) with the Neuropsychiatric Inventory Apathy subscale against Diagnostic Criteria of Apathy. J Am Med Dir Assoc 2012; 13:308.e1–308.e6
21. de Haan R, Limburg M, Schuling J, et al: [Clinimetric evaluation of the Barthel Index, a measure of limitations in daily activities]. Ned Tijdschr Geneeskd 1993; 137:917–921
22. Sulter G, Steen C, De Keyser J: Use of the Barthel index and modified Rankin scale in acute stroke trials. Stroke 1999; 30: 1538–1541
23. Fries BE, Simon SE, Morris JN, et al: Pain in U.S. nursing homes: validating a pain scale for the minimum data set. Gerontologist 2001; 41:173–179
24. Pieper MJ, Achterberg WP, Francke AL, et al: The implementation of the serial trial intervention for pain and challenging behaviour in advanced dementia patients (STA OP!): a clustered randomized controlled trial. BMC Geriatr 2011; 11:12
25. Lynch J, Mead G, Greig C, et al: Fatigue after stroke: the development and evaluation of a case definition. J Psychosom Res 2007; 63:539–544
26. Paquay L, De Lepeleire J, Schoenmakers B, et al: Comparison of the diagnostic accuracy of the Cognitive Performance Scale (Minimum Data Set) and the Mini-Mental State Exam for the detection of cognitive impairment in nursing home residents. Int J Geriatr Psychiatry 2007; 22:286–293
27. de Jonghe JF, Kat MG, Kalisvaart CJ, et al: [Neuropsychiatric inventory questionnaire (NPI-Q): A validity study of the Dutch form]. Tijdschr Gerontol Geriatr 2003; 34:74–77
28. Morris JN, Belleville-Taylor P, Fries BE, et al: InterRAI Long-Term Care Facilities (LTCF) Assessment Form and User's Manual, 9.1. Washington, DC, interRAI, 2006
29. Twisk JWR: Applied Multilevel Analysis. A Practical Guide. Cambridge, Cambridge University Press, 2006
30. Marin RS: Differential diagnosis and classification of apathy. Am J Psychiatry 1990; 147:22–30
31. Brodaty H, Sachdev PS, Withall A, et al: Frequency and clinical, neuropsychological and neuroimaging correlates of apathy following stroke—the Sydney Stroke Study. Psychol Med 2005; 35:1707–1716
32. Hama S, Yamashita H, Yamawaki S, et al: Post-stroke depression and apathy: interactions between functional recovery, lesion location, and emotional response. Psychogeriatrics 2011; 11:68–76
33. Barnhart WJ, Makela EH, Latocha MJ: SSRI-induced apathy syndrome: a clinical review. J Psychiatr Pract 2004; 10:196–199
34. Murakami T, Hama S, Yamashita H, et al: Neuroanatomic pathways associated with poststroke affective and apathetic depression. Am J Geriatr Psychiatry 2013; 21:840–847
35. Glader EL, Stegmayr B, Asplund K: Poststroke fatigue: a 2-year follow-up study of stroke patients in Sweden. Stroke 2002; 33: 1327–1333
36. Duncan F, Wu S, Mead GE: Frequency and natural history of fatigue after stroke: a systematic review of longitudinal studies. J Psychosom Res 2012; 73:18–27
37. Smets EM, Garssen B, Bonke B, et al: The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res 1995; 39:315–325
38. Verkaik R, Francke AL, van MB, et al: The effects of a nursing guideline on depression in psychogeriatric nursing home residents with dementia. Int J Geriatr Psychiatry 2011; 26: 723–732
39. Verkaik R, Francke AL, Smalbrugge M: [The Pleasant-Events-Method after a stroke]. TvZ 2013; 3:48–51
40. Spiegel DR, Kim J, Greene K, et al: Apathy due to cerebrovascular accidents successfully treated with methylphenidate: a case series. J Neuropsychiatry Clin Neurosci 2009; 21:216–219