Stroke
Journal of the American Heart Association

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Stroke. 2009;40:3299-3307; originally published online August 27, 2009;
doi: 10.1161/STROKEAHA.109.554410
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

A Longitudinal View of Apathy and Its Impact After Stroke

Nancy E. Mayo, PhD; Lesley K. Fellows, MD, DPhil; Susan C. Scott, MSc;
Jill Cameron, PhD; Sharon Wood-Dauphinee, PhD

Background and Purpose—Stroke survivors are often described as apathetic. Because apathy may be a barrier to participation in promising therapies, more needs to be learned about apathy symptoms after stroke. The specific objective was to estimate the extent to which apathy changes with time over the first year after stroke and the impact of apathy on recovery.

Methods—The Apathy Assessed cohort was formed from stroke survivors participating in a longitudinal study of health-related quality of life after stroke. A family caregiver completed an apathy questionnaire by telephone at 1, 3, 6, and 12 months after stroke (n=408). Group-based trajectory modeling and ordinal regression were used to identify distinctive groups of individuals with similar trajectories of apathy over the first year after stroke and predictors of apathy trajectory.

Results—Both 3- and 5-group trajectory models fit the data. We used the 5-group model because of the potential to further explore the apathy construct. The largest group (50%) had low apathy and 33% had minor apathy that remained stable throughout the first year after stroke. A small proportion (3%) of the study sample had high apathy that remained high. Two other groups of almost equal size (7%) showed worsening and improving apathy. Poor cognitive status, low functional status, and high comorbidity predicted higher apathy. High apathy had a significant negative effect on physical function, participation, health perception, and physical health over the first 12 months after stroke.

Conclusion—Some degree of apathy was prevalent and persistent after stroke and was predicted by older age, poor cognitive status, and low functional status after stroke. Even a minor level of apathy had an important and statistically significant impact on stroke outcomes. **(*Stroke*. 2009;40:3299-3307.)**

Key Words: depression ■ function ■ motivation ■ stroke

To borrow a phrase from William James,[1] "everyone knows what apathy is." Family members caring for persons with stroke certainly know it when they see it, and they see it often. Stroke survivors are commonly described as having lost interest, seeming unmotivated, being unable to get going, or being content to just sit there.[2] From a clinical perspective, apathy is often used as an umbrella term to refer rather generally to a lack of emotion, interest, or concern.[3] Such symptoms, alone or in combination, pose challenges for rehabilitation and social re-engagement after stroke.[4]

Van Reekum et al[5] in a 2005 review of detection, pathophysiology, and treatment of apathy suggested a definition of apathy as an absence of responsiveness to stimuli demonstrated by a lack of self-initiated actions. Marin[3] defined apathy syndrome as a decrease in goal directed behavior attributable to loss of motivation. Whereas such general definitions have a commonsense appeal, it is highly likely that "apathy" so-defined refers to a heterogeneous set of difficulties, with different causes and outcomes.

Operational issues notwithstanding, apathy is recognized as a symptom in many neurological illnesses and is particularly prominent in disorders that affect the frontal lobes, the basal ganglia, or the links between them.[5,6] Beyond this observation, little is known about the neural mechanisms underlying this behavior. Apathy can also be a feature of psychiatric illness, most notably depression. Existing work has shown that depressed mood and apathy can be disentangled in neurological conditions,[6,7] arguing that the 2 represent distinct, albeit potentially related, constructs.[5]

Despite the recognition of apathy as a limiting factor to rehabilitation,[8] and the neuroscience work arguing that there are definable neural systems that, when damaged, could lead to apathy, there are remarkably few studies of apathy after stroke and these are summarized in Table 1. Existing work suggests that apathy after stroke ranges from 19% to 55%. Further, there is some suggestion that apathy may change over time, although the only study[2] involved 3 separate cross-sectional samples of convenience, preventing any

Received April 2, 2009; accepted May 6, 2009.

From Division of Clinical Epidemiology (N.E.M., S.C.S., S.W.-D.), Department of Medicine and School of Physical and Occupational Therapy (N.E.M., S.W.-D.), Joint Department of Epidemiology and Biostatistics and Occupational Health (N.E.M., S.W.-D.), Department of Neurology & Neurosurgery (L.K.F.), McGill University Health Center, Montreal, Quebec, Canada; Department of Occupational Science and Occupational Therapy (J.C.), University of Toronto, Toronto, Canada; Toronto Rehabilitation Institute (J.C.), Toronto, Canada.

Correspondence to Nancy Mayo, Division of Clinical Epidemiology, Royal Victoria Hospital, 687 Pine Avenue West, R4.17, Montreal, Quebec, Canada, H3A 1A1. E-mail nancy.mayo@mcgill.ca

Stroke **is available at http://stroke.ahajournals.org** **DOI: 10.1161/STROKEAHA.109.554410**

Table 1. Summary of the Literature on Apathy After Stroke

Author	Sample Size	Apathy Index, Respondent	Type and Time After Stroke	Time After Stroke	% With Apathy	% With Depression and Apathy
Mayo (this study)	408	Apathy Index, family caregivers	Ischemic or hemorrhagic	1, 3, 6, and 12 mon	20%*	8%
Carota 2005[9]	273	EBIF, nurses	Uncomplicated ischemic	Days after stroke	48%	21%
Hama 2005[34]	237 (patient)	Starkstein	Ischemic or hemorrhagic	7–90 days	40%	19%
	219 (observer)	Family caregivers			19%	13%
Brodaty 2005[35]	135	Marin's AES	Ischemic	3–6 mon	27%	17%
Angelelli 2004[2]	124	NPI	Ischemic	2, 6, or 12 mon	27%	Not reported
Starkstein 1993[36]	80	Starkstein		10 days	23%	20%
Okada 1997[37]	40	Starkstein	Subcortical infarction	0–5 yr	50%	20%
Glodzik-Sobanska 2005[38]	31	Starkstein	Ischemic	7–12 days	42%	23%
Yamagata 2004[39]	29	Starkstein	Subcortical infarction	1–10 mon	55%	7%

AES indicates Apathy Evaluation Scale[3]; EBIF, Emotion Behaviour Index Form[40]; NPI, Neuropsychiatric Inventory[41]; Starkstein's Apathy Scale.[36]
*Using ≥3 on the 6-Item Apathy Index as the cut-point for apathy.

strong claims about time course. The other studies reported in Table 1 examined only a single point in time and varied widely with respect to time since stroke and stroke type. There was also substantial variability in measurement tools and mode of evaluation (self-report or observer-rated).

Existing work does support the view that apathy and depression are distinct (if sometimes overlapping) constructs. Angelelli et al[2] found that 27% of 124 persons with stroke were considered to have apathy, and 61% had depression. The study by Carota et al[9] found a different pattern, with apathy more common (48%) than either major (11%) or minor (23%) depression.

Does apathy after stroke matter? Common sense would suggest that it might. One of the current priorities for stroke research in Canada is community participation,[10] now recognized as a key factor contributing to quality of life after stroke.[11] In addition, there are promising new rehabilitation therapies being developed and tested, but persons need to be highly motivated to participate.[12,13] Apathy may be a barrier to participation in these initiatives. If so, it needs to be anticipated, recognized, and treated. For this to occur, more needs to be learned about the nature of apathy symptoms after stroke, including the time course of their emergence, and their relationship to recovery of function. The specific objectives were to estimate the extent to which apathy changes with time over the first year after stroke and the impact of apathy on recovery.

Materials and Methods

Source of Data

The data for this analysis came from a longitudinal study of health-related quality of life involving 678 persons after stroke and, when possible, their caregivers (n=410). Between 2003 and 2004, subjects were recruited from 10 acute-care hospitals in Montreal (Quebec City), Toronto (Ontario), and London (Ontario) and were followed by telephone interviews at 1, 3, 6, and 12 months after stroke. For people who could not respond for themselves, proxy responders were accepted.

Subjects

Those enrolled were people with first confirmed stroke who spoke English or French or who had significant others who were fluent in either of these languages, who provided written informed consent, and who did not have severe comorbidity that was likely to dominate the pattern of care and result in serious health decline or death within the study period. Persons discharged directly to long-term care were excluded.

The study population for this research question was the subset with a caregiver who completed the questionnaire identifying the presence of behaviors indicative of apathy. Of the 410 caregivers, 408 completed at least 1 set of ratings on the stroke subject; 35 (8.6%) were lost by 3 months, half because of death or institutionalization of the stroke subject and half because of unwillingness to participate; 65% were followed-up for the full year. The stroke survivors (n=408) assessed by their caregivers formed the Apathy-Assessed (AA) cohort.

Measures

Apathy of the stroke survivors was measured using 6 items drawn from the Williams Brain Impairment Behavior Scale[14] as modified by Cameron et al.[15] The caregiver rates the extent to which behavioral changes are observed in the person for whom they are providing care. Polychoric correlations (for ordinal items) and parallel analysis identified that these 6 items formed a single factor.[16] Recently, Cameron et al[15] completed further analyses of this scale in survivors of first and subsequent stroke and identified an apathy factor comprising 5 of the 6 items used here but the sixth item ("does not try very hard") just missed the critical value for retention.

An index was created by assigning a score of 0 for original response levels of none or rarely, a score of 1 for a response of moderately, and a score of 2 for a response of often or always. This rescoring was indicated because a Rasch Analysis[17] revealed that extreme response options were not used in a consistent manner. Thus, the 6-Item Apathy Index had a range between 0 and 12, with higher scores indicating more apathy. Using content referencing, the presence of clinically relevant apathy was defined as a score of ≥3 that could be obtained by scoring moderately affected on half of the items or often or always affected if only 2 items are endorsed.

Recovery after stroke was measured using the Stroke Impact Scale (SIS),[18] Preference-Based Stroke Index,[19] Measuring Outcomes Study Short-Form 36 item questionnaire (SF-36),[20] and the EuroQuol,[21] all of which were completed by the patient or, on occasion, by their caregiver as proxy at 1, 3, 6, and 12 months after stroke.

Other explanatory variables included stroke severity as measured by the Canadian Neurological Scale,[22] activities of daily living capacity (Barthel Index), side of lesion, age, and gender, all measured in hospital, as well as variables measured at each interview. Cognition was measured by the telephone version of the Mini-Mental Status Examination,[23,24] and comorbidity was measured using the Charlson Index,[25] with hemiplegia and dementia eliminated from the scoring algorithm.

Table 2. Comparison of Members of the AA Cohort to Excluded Stroke Subjects on Stroke-Related Factors

	AA Cohort (n=408)			Excluded Stroke Subjects (n=268)			
	N 408	Mean (or %)	SD	N 268	Mean (or %)	SD	*P*†
Women	167	40.9		137	51.1		0.009
Men	241	59.1		131	48.9		
Age at stroke (mean, SD)	406	66.5	14.6	268	68.5	15.2	0.083
<45	39	9.6		24	9.0		0.663
45–64	125	30.8		78	29.1		
65–84	208	51.2		136	50.8		
≥85	34	8.4		30	11.2		
Side of lesion	408	.	.	268			
Left	177	43.4		115	42.9		0.562
Right	197.	48.3		127	47.4		
Bilateral lesion	18.	4.4		18	6.7		
Not recorded	16.	3.9		8	3.0		
Stroke Severity: Canadian Neurological Scale: 1.5 (worst)–11.5 (best)							
Mean	400	8.3	2.6	265	8.8	2.3	0.012
Severe: 0–5	68	17.0		25	9.4		0.049
Moderate-high: 5.5–9	153	38.3		107	40.4		
Moderate-low: 9.5–10.5	101	25.3		72	27.2		
Mild: 11–11.5	78	19.5		61	23.0		
Functional Status: Barthel Index (0–100)							
Mean	401	73.5	26.1	263	76.4	25.4	0.156

The SIS is a disease-specific evaluative instrument that measures the impact of stroke in multiple domains: physical, emotional, memory/thinking, communication, and social participation.[18,26,27] Each is scored out of 100, with higher scores indicating higher function.

The SF-36 is a generic measure of health status and includes 8 multi-item scales measuring physical functioning (10 items), role limitations attributable to physical health problems (4 items), bodily pain (2 items), general health perceptions (5 items), vitality (4 items), social functioning (2 items), role limitations attributable to emotional problems (3 items), and mental health (5 items). Response choices vary and range from 2- to 6-level scales. Subscale scores range from 0 to 100, with higher scores indicating better health states. Physical component summary and mental health component summary, standardized to have a mean of 50 and SD of 10, can be derived from the items.[20] The mental health component summary has been shown to be useful in screening for psychiatric conditions, with a cut-off score of 42 associated with a sensitivity of 74% and a specificity of 81% in detecting patients with a diagnosed depressive disorder.[28]

The EuroQol has 2 parts, the EQ-5D index and the EQ-5D visual analogue scale (VAS). The index is a 5-item standardized generic measure of health referring to EuroQol with domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The VAS is a 0 to 100 thermometer scale that assesses self-perceived health status. Anchors on the thermometer are 0 (worst possible health state) and 100 (best possible health state). Both the EQ-5D index and EQ-5D VAS assess health on that day.[21]

Statistical Methods

Members of the AA cohort were compared to excluded stroke subjects using *t* tests for variables measured on a continuous scale and χ^2 tests for variables measured on a categorical scale. To minimize potential bias arising from persons dropping out of the cohort, multiple imputation was performed[2,29,30] on the longitudinal data. To impute the missing data, 10 imputed data sets were created. Imputation was based on the data arising from key measured variables age, gender, Barthel index, Canadian Neurological Scale, side of lesion, and comorbidity measured while the subject was still in hospital, as well as values on the health questionnaires at each interview: vitality, mental health, physical component summary, and mental health component summary from the SF-36; memory, participation, and physical score from the SIS, the Mini-Mental, and the EQ-5D VAS. All analyses were performed using SAS version 9.1. Means and regression using imputed data were combined through the SAS procedure, proc mianalyse.

Group-based trajectory modeling,[31,32] a form of finite mixture modeling, was used to identify distinctive groups of individuals with similar trajectories of apathy over the first year after stroke. A model for censored normal data were used, with the calculated apathy score as outcome regressed against the time from stroke. Fit statistics and posterior probabilities of group membership were used to compare models with different numbers of trajectory groups, as well as models including time as linear and quadratic. Statistics presented for imputed data are weighted averages of results with the 10 imputed datasets. Bayesian information criterion are given based on 1 degree of freedom (df) per subject (rather than 1 df per interview).

Predictors of apathy were examined using ordinal regression;[33] the cumulative OR model was used, yielding OR and 95% CI. Homogeneity of the OR across changing cut-points on the Apathy Index was confirmed using the score test performed in each of the 10 imputed datasets.

Growth curve modeling was used to demonstrate the association of apathy on recovery after stroke. SAS proc mixed was used with multiple results from imputed datasets combined using SAS proc mianalyze. Time was modeled as a random effect with linear and quadratic factors. Trajectory groups were considered as fixed effects. To determine whether their association with the outcome varied over time, interactions with time were considered, as were

Table 3. Distribution of Ratings on Apathy Questions

	1 Month			3 Months			6 Months			12 Months		
	N	%	%I	N	%	%I	N	%	%I	N	%	%I
Does not want to do anything												
R	272	78.6	77.5	229	76.1	74.2	225	80.4	77.4	215	82.1	78.2
M	42	12.1	13.3	33	11.0	12.6	32	11.4	13.4	29	11.1	13.8
O	32	9.2	9.2	39	13.0	13.1	23	8.2	9.2	18	6.9	8.0
Waits for someone to do things that he/she can do for self												
R	302	87.3	86.5	254	84.4	83.2	240	85.7	83.1	225	85.9	81.6
M	27	7.8	8.4	25	8.3	9.5	23	8.2	10.5	20	7.6	10.6
O	17	4.9	5.1	22	7.3	7.3	17	6.1	6.4	17	6.5	7.8
Acts as if he/she has no interest in anything												
R	283	81.8	80.9	237	78.7	77.1	235	83.9	80.6	216	82.4	78.1
M	31	9.0	10.1	28	9.3	10.8	22	7.9	10.8	25	9.5	12.8
O	32	9.2	9.1	36	12.0	12.1	23	8.2	8.6	21	8.0	9.0
Just sits and watches												
R	282	81.5	79.9	233	77.4	76.3	237	84.6	80.7	221	84.4	78.0
M	25	7.2	9.0	29	9.6	11.2	18	6.4	10.1	20	7.6	12.0
O	39	11.3	11.1	39	13.0	12.6	25	8.9	9.2	21	8.0	9.9
Difficulty becoming interested in activities												
R	273	78.9	78.2	218	72.4	72.4	225	80.4	77.4	207	79.0	74.5
M	33	9.5	10.6	38	12.6	13.5	30	10.7	12.6	26	9.9	13.8
O	40	11.6	11.3	45	15.0	14.2	25	8.9	9.9	29	11.1	11.7
Does not try very hard												
R	323	93.4	93.1	268	89.0	87.7	254	90.7	89.1	233	88.9	85.6
M	13	3.8	4.4	20	6.6	7.8	15	5.4	7.2	19	7.3	10.2
O	10	2.9	2.5	13	4.3	4.5	11	3.9	3.7	10	3.8	4.3
6-Item Apathy Index												
Mean		1.5	1.5	301	1.9	1.9	280	1.4	1.6	262	*1.4*	*1.7*
SD/SE		2.7	0.13		3.0	0.16		2.6	0.13		2.7	0.15

I indicates imputed proportion using multiple imputation for missing data; M, moderately; O, often; R, rarely; SE, standard error for imputed data.
6-Item Apathy Index is scored from 0 to 12, with higher scores indicating more apathy.

interactions with confounders. For graphical display, growth models were drawn for fixed values of specific covariates. The values were chosen to be representative of the larger group.

Results

The AA cohort and the excluded group differed on the number of interviews completed and also on gender and stroke severity, as shown in Table 2. There were proportionally more men than women assessed for apathy (59% vs 49%), likely because the majority of the caregivers (69%) were women. The mean stroke severity in the excluded group was 8.8 (SD, 2.3), indicating less severe stroke, compared with 8.3 (SD, 2.6) in the AA cohort; 17% in the AA cohort had severe stroke compared with 9.4% in the excluded cohort. The AA cohort had slightly more interviews than the excluded group (3.2; SD, 1.0 vs 3.0; SD, 1.2). The average age in the AA cohort was 2 years younger than the excluded group ($P=0.08$) but their distributions were similar.

The distribution of responses on the 6 questions that asked about motivation is shown in Table 3 for both observed and imputed data. At 1 month after stroke, the proportion of subjects rated by their caregivers as showing indications of apathy ranged from 7% ("does not try very hard") to 21% ("does not want to do anything" and "difficulty becoming interested in activities"). Again, imputed proportions for the "rarely" category are lower than observed, indicating that those with missing data were more likely to have apathy. The discrepancy between observed and imputed data widened over time, illustrating that persons with apathy were increasingly excluded as time went on. The average value for the 6-Item Apathy Index is also presented. The mean score was 1.5 at the 1-month interview and 1.4 at the 12-month interview. Imputed means are higher than observed, indicating that those who dropped out had higher apathy. As the proportion of missing data increased over time, so did the discrepancy between observed and imputed scores.

For the trajectory analysis, the optimal number of groups was not clear, because both the 5-group and the 3-group model showed adequate fit. Table 4 presents the results of the

Table 4. Description Apathy Trajectory Groups

Group	Intercept*	%	Posterior Probability of Group Membership: Mean (SD)	Posterior Probability of Group Membership: Minimum–Maximum
3-group model				
Low	0.2	54.2	0.93 (0.11)	0.57–0.99
Minor	2.4	37.0	0.89 (0.14)	0.53–1.00
High	7.3	8.9	0.91 (0.12)	0.61–1.00
5-group model				
None	0.1	50.3	0.90 (0.12)	0.56–0.98
Minor	2.1	33.1	0.84 (0.13)	0.44–0.98
Worsening	2.4	6.6	0.79 (0.17)	0.44–0.99
Improving	5.6	6.8	0.75 (0.16)	0.46–0.98
High (4)	8.6	3.1	0.89 (0.15)	0.54–1.00

Missing data imputed.

*The scale of the 6-Item Apathy Index ranged from 0 to 12.

Bayesian Information Criterion (408 df) was −2477 for 3-group model and −2481 for 5-group model. Akaike Information Criterion was −2461 for 3-group model and −2449 for 5-group model. Lower values indicate better fit. Statistics given have been averaged across 10 imputed datasets. Proportions are calculated based on assignment to the group with the highest probability.

trajectory analyses. Both the 3- and 5-group models showed equivalent fit on Bayesian information criterion with all subjects combined; the 3-group model fit significantly better using Bayesian information criterion for the reduced sample (n=408) and the 5-group model fit significantly better on the Akaike information criterion. The mean apathy at first interview (intercept) for each of the groups is also shown, and for the low, minor, and high groups, these are closely similar.

Because this was the first time that apathy has been examined longitudinally, the 5-group model was chosen because of the potential to further explore the apathy construct. This model, shown in Figure 1, included 3 groups showing stable trajectories over time but at different levels of apathy, with 1 group showing a linear increase and another group showing a linear decrease. The proportions indicated on the graph represent theoretical proportions derived from the model rather than calculated proportions, which are presented in Table 4, for both the 3- and 5-group trajectory models, based on assigning persons to the group with the highest posterior probability.

Characteristics of members of the AA cohort in hospital and at first interview are presented in Table 5 according to apathy group membership. The results of the ordinal regression analysis showed that, adjusted for age and gender, poor cognitive status (<75/100; OR, 1.9; 95% CI, 1.1–3.3), low functional status before discharge from hospital (Barthel Index <65; OR, 1.8; 95% CI, 1.1–3.1), and high comorbidity (Charlson Index, 4–6; OR, 2.1; 95% CI, 1.0–4.3) were significant predictors of higher apathy.

Apathy and depression were also related but not synonymous. Persons were classified with depression or not based on a cut-off score on the mental health index of the SF-36 of 52.[28] At 1 month, 23% of the AA cohort scored in the "at risk" range for depression using this criterion, but only 20%

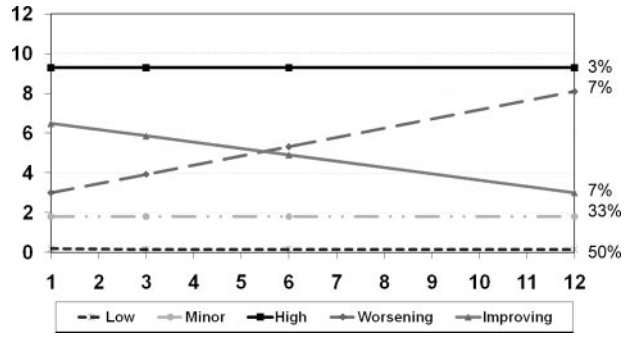

Figure 1. The 5-group trajectory model for apathy over the first year after stroke.

scored in the clinically relevant apathy range, using 3 of 12 as a cut-off. Only 8% of the cohort was concordant for both depression and apathy using these criteria. Figure 2 shows the association between apathy and recovery (A, physical function; B, participation; C, health perception; and D, physical health). Table 6 provides the regression parameters associated with the curves shown. For all models, recovery occurred nonlinearly over time (time and time^2 terms were significant), with higher rates in the first 6 months after stroke and slowing thereafter. The level of early recovery (intercept) was significantly associated with activities of daily living capacity at hospital discharge (Barthel Index). All models were also adjusted for gender, stroke severity (Canadian Neurological Scale), comorbidity (Charlson score), age, and the impact of age over time (curves varied over time by age group). Female gender was significantly associated with lower early physical function (β SIS physical: −3.3:) and physical health (β SF-36 physical component summary: −3.4).

For physical function measured by the SIS physical and shown in Figures 2, there is a clear demarcation in impact between low (referent trajectory) and minor apathy. The β associated with minor apathy, −8.0 (95% CI, −12.8–−3.1) indicates that people with minor apathy scored, on average, 8 points lower on the SIS physical subscale than people with low apathy. High, worsening, and improving apathy, although having a strong negative association with physical function, are indistinguishable from each other (β range, −14.2–−15.4).

For participation, even minor apathy had a strong negative association with recovery of this construct (β=−10.1; 95% CI, −15.0–−15.3), which is closely similar to the impact of worsening apathy (β=−11.8; 95% CI, −21.7–−2.0). For health perception measured by the EQ-VAS, the 5 apathy groups are clearly distinguishable regarding their impact on this outcome, with high apathy associated with the poorest perceived health over time. Finally, for physical health as measured by the physical component summary of the SF-36, as apathy worsened, physical health decreased over time, as shown by the significant interaction for worsening*time.

Discussion

Given the importance of motivation for achieving life goals in general and for meeting the challenges of the recovery process, it is surprising that apathy has received so little attention after stroke. In the work that has been performed to

Table 5. Characteristics of Members of the AA Cohort According to Apathy Trajectory Group

	Apathy Trajectory Group									
	Low		Medium		High		Worsening		Improving	
	50.3%		33.1%		3.1%		6.6%		6.8%	
Proportion	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Apathy score	0.2	0.1	1.7	0.3	8.6	0.9	1.9	0.6	6.9	0.9
Age at stroke	66.1	1.1	66.2	1.3	67.2	5.4	65.6	3.2	71.6	3.0
Barthel Index	76.8	1.9	69.9	2.7	62.5	9.9	69.9	6.7	70.5	8.1
Canadian Neurological Scale	8.3	0.2	8.3	0.3	8.3	0.9	8.0	0.6	8.6	0.6
Charlson Comorbidity Index	1.4	0.1	1.7	0.1	1.9	0.4	1.6	0.3	1.6	0.3
Mini-Mental Status Examination	89.0	1.2	84.3	2.0	86.6	5.9	85.9	4.3	79.0	5.4
SF-36										
Physical component summary	38.0	0.7	33.1	1.0	30.6	4.1	32.5	2.6	31.9	2.3
Mental health component summary	44.9	0.8	39.5	1.2	35.0	4.7	37.7	3.8	32.8	3.1
Physical	69.3	1.9	60.0	2.9	47.5	9.3	58.6	7.3	51.0	7.2
Vitality	47.1	1.8	41.8	2.4	38.0	10.2	47.6	7.1	31.0	5.4
Mental health	74.6	1.5	67.5	2.4	56.7	8.7	65.0	6.5	55.0	5.6
Stroke Impact Scale										
Physical	69.3	1.9	60.0	2.9	47.5	9.3	58.6	7.3	51.0	7.2
Memory	88.9	1.2	77.7	2.5	79.1	6.7	80.7	5.5	64.6	6.4
Participation	53.1	2.1	44.8	2.8	42.8	10.4	46.0	7.6	40.4	6.8
EQ-VAS	71.0	1.5	62.7	2.4	42.0	9.9	54.6	6.7	58.1	6.0

Canadian Neurological Scale and Barthel Index were recorded in hospital; all others were recorded at 1 month after stroke.

date, the prevalence of apathy ranged from 19% to 55%. The group-based trajectory method estimated that 50% of the population were outside of the "low apathy" group consistently over 1 year. The literature, shown in Table 1 (which included our study), estimated that depression was coexistent with apathy in 17% to 69% of the stroke survivors studied. Our estimate was 8%.

In addition to a relatively large sample size and the recruitment from an inception cohort, there are several unique features of this study. This was the only study found that had serial measures of apathy over time and, similar to 2 other studies,[9,34] that did not rely on the stroke survivor's own report of apathy, which may not be accurately or consistently rated over time. In addition, modern statistical methods were used to deal with the challenge of missing data. The effect of imputation for missing data is to increase reported apathy and lower the other scores, illustrating the bias that occurs if missing data are excluded. People with worse apathy scores tend to be the persons with missing data. Hence excluding them provides artificially better mean scores if only those with complete data are allowed to represent the entire group including those with missing data. Also, the sample included was very similar to the larger stroke population (Table 2), indicating these results are likely generalizable.

Even though this was an inception cohort in that all persons with stroke were enumerated at the time of stroke, we were able to estimate prevalence of apathy only as we followed-up only those persons who returned to the community. New occurrences of apathy over the first year after stroke could only be identified from among those with no or low apathy at first interview. In this study, we felt the group-based trajectory method was the best way of estimating new occurrences and this number was low; only 6.6% of the cohort was classified into the group of increasing apathy over time. This method indicated that the majority of people (50%) with stroke were considered by their caregivers to demonstrate apathetic behaviors only rarely (low apathy), 33% showed minor apathy, and 3% showed high apathy, and that the extent of apathetic behavior remained fairly stable over the first year after stroke. Only 7% showed any sign that apathy improved over time. This finding has several potential explanations. It may be a statistical artifact of the 5-group model that we chose over the 3-stable group model. We chose the 5-group model because both models fit the data equally well and the 5-group model provided more scope for discussion, given how little is known about apathy. Perhaps the rehabilitation process does not offer enough intervention targeted at reducing apathy and this is why so few people improve. Alternatively, apathy may not be a construct that is amenable to change—akin to a trait rather than a state. Finally, apathy, as measured here with general questions, may be attributable to multiple processes with more dynamic time courses: some recovering, eg, those cases related to brain injury in some direct way, and others worsening, eg, those cases related to the effects of coping with new disability, psychological, or psychiatric issues, with the net effect a "stable" process.

The validity of the 5-group apathy model is supported by the observations that 3 of the 4 outcomes showed 5 distinct

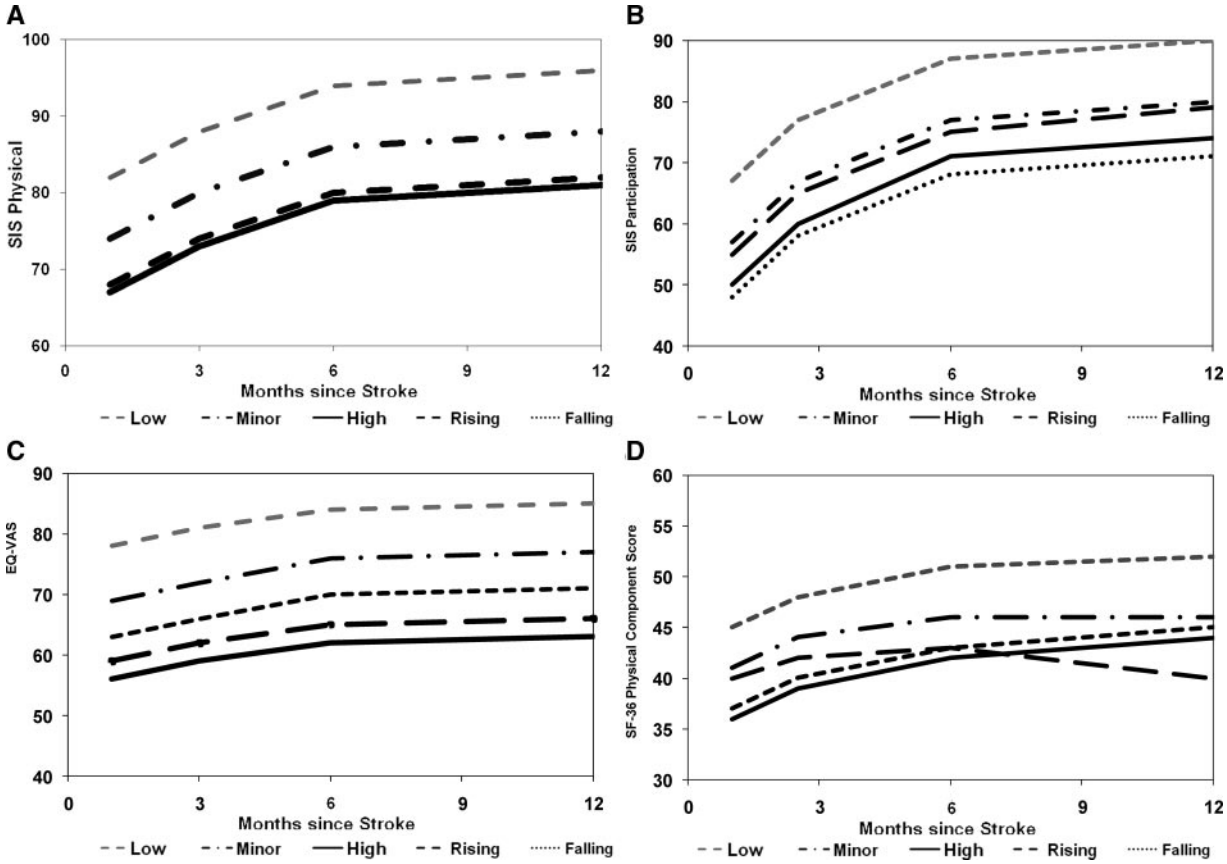

Figure 2. Growth curves showing the effect of apathy trajectory on four outcomes. A, Physical function as measured by SIS physical. B, Participation (SIS participation). C, Health perception (EQ-5D VAS). D, Physical health (SF-36 physical component summary). Lines are drawn for each apathy trajectory are for men aged 65 to 75 years, with a Canadian Neurological Scale score of 8.5 indicating moderate stroke, Charlson Index 2, and Barthel Index of 100, measured in hospital.

recovery patterns that were associated with on apathy. Only physical function depended on only 3 of the 5 apathy trajectories. Also, although low and minor apathy did not differ much in terms of absolute score on the Apathy Index, minor apathy was associated with poorer recovery across all outcomes. Support for the validity of changing apathy is provided by the observation that increasing apathy over time was associated with decreased physical health.

The information regarding lesion location available in this dataset was relatively coarse, making it difficult to make strong claims about the relation between site of damage and apathy. With that proviso, there was no striking commonality in lesion location among patients in the high apathy group. That group included only 1 patient with an isolated frontal lobe stroke and was otherwise split between middle cerebral artery territory strokes, and ischemic or hemorrhagic strokes affecting the basal ganglia. Interestingly, 3 patients in this group had infratentorial damage affecting the cerebellum or pons. At the least, this argues against the clinical stereotype of apathy being strongly (and specifically) associated with frontal, and particularly medial, frontal lobe damage. To the degree that apathy can be localized based on these data, the results are more supportive of a distributed fronto-striatal network (and perhaps fronto-cerebellar network) supporting motivated behavior, consistent with at least 1 recently proposed model.[6]

The measure of apathy used here has several limitations and if the area of apathy and motivation after stroke is to be advanced further, research into the measurement of this construct needs to be undertaken. The 6-Item Apathy Index used in this study has the advantage of having a caregiver to provide the rating, but it has not been validated as a stand-alone measure. The items were drawn from a much longer index of behavior changes, although the items formed a single factor. Four of the items ask about interest and 2 items relate to effort. One explanation for our finding that persons with stroke have stable apathy scores over time is that ≥1 of these 6 items may not be modifiable. If a different set of questions had been asked, a different set of trajectories might have been observed. It may also be that caregivers' ratings of behaviors may not change over time, even though the patient does change. This may be a feature of the construct or a feature of the measurement method.

Starkstein's Apathy Scale is an alternative, widely used instrument that has a total of 14 items, 8 of which came from the original Marin's Apathy Evaluation. These items cover constructs such as interest, effort, concern, mood, energy and drive, boredom, and future plans, in contrast to the apathy items we had available for this study that assess interest and effort only. On the Starkstein scale, the subjects rate themselves, on the measure used here, and caregivers provided the rating. Self-rating may be prob-

Table 6. Parameter Estimates From the Growth Curve Model Showing the Impact of Apathy Trajectory on Recovery of Key Outcomes Over 12 Months After Stroke

Outcome	β	95% CI	P
SIS Physical			
Low	Referent		
Minor	−8.0	−12.8–−3.1	<0.01
High	−15.4	−25.9–−5.0	<0.01
Worsening	−14.2	−21.8–−6.6	<0.01
Improving	−15.3	−22.3–−8.3	<0.01
SIS Participation			
Low	Referent		
Minor	−10.1	−15.0–−5.3	<0.01
High	−16.5	−30.1–−3.0	0.02
Worsening	−11.8	−21.7–−2.0	0.02
Improving	−19.3	−27.4–−11.2	<0.01
EQ-VAS			
Low	Referent		
Minor	−8.4	−11.6–−5.1	<0.01
High	−22.0	−32.0–−12.0	<0.01
Worsening	−18.8	−25.9–−11.7	<0.01
Improving	−14.4	−23.5–−5.2	<0.01
SF-36 PCS			
Low	Referent		
Minor	−3.6	−5.7–−1.5	<0.01
High	−9.1	−16.0–−2.3	0.01
Worsening	−4.4	−9.1–0.4	0.07
Improving	−8.3	−12.0–−4.6	<0.01
Minor*time	−0.3	−0.5–0.01	0.06
Worsening*time	−0.8	−1.4–−0.1	0.03

All estimates are adjusted for age, gender, stroke severity (Canadian Neurological Scale), extent of limitation in basic activities of daily living (Barthel Index), and comorbidity (Charlson Index) in hospital, and include parameters measuring the changing association of age and recovery over time.

lematic for people with stroke. For example, 1 of the questions in the Starkstein scale asks, "Would you consider yourself to be apathetic?" We have noted that in interviewing persons with stroke, few knew what the word "apathetic" actually meant. Some of the stroke survivors thought it was a good quality, perhaps confusing the term with "sympathetic" or "empathetic." Finally, the response options on the Starkstein scale are not at all, slightly, some, and a lot. Many of the stroke patients we have subsequently interviewed could not sort out whether "slightly" was more or less than "some," particularly when they were asked about a negative construct, eg, indifference. Also, people with stroke may not have the insight to be able to recognize that they have these feelings or behaviors.

The results presented in Table 5 indicate that there were only a few predictors of apathy as measured by the index we used: low cognitive status, low initial function, and high comorbidity. Starkstein[36] also identified cognitive impairment and limitations in activities of daily living, as well as age, as associated with apathy, but the Starkstein group was somewhat younger (mean age, 61 years) than the cohort reported here (mean age, 66.5 years). We found that persons whose apathy decreased over time were ≈5 years older than members of the other apathy groups.

The main limitation of the study is the way in which apathy was measured, but, currently, none of the available measures of apathy would be considered optimal by modern psychometric standards, indicating that this important construct warrants further study. In addition, it is not clear that after a stroke it is possible or even necessary to disentangle fully the related emotional/psychological impacts of stroke on apathy, mood, anxiety, fatigue, and self-efficacy. A more relevant construct to conceptualize, measure, and treat may be emotional reserve—those emotional resources persons have at their disposal to combat stressors. Having a stroke, recovering from a stroke, and getting on with the rest of life after a stroke would be considered by many to be stressors. Emotional reserve may be a factor distinguishing those who seem to master their health condition and disability from those who do not. Apathy is clearly 1 key ingredient that has been underinvestigated in stroke, and this article shows apathy can be quantified and that it impacts strongly on stroke recovery.

Sources of Funding

Funded by the Canadian Stroke Network.

Disclosures

None.

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