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## Original Study

# The Prevalence and Determinants of Neuropsychiatric Symptoms in People With Acquired Brain Injury in Nursing Homes



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## A B S T R A C T

**Keywords:**

Acquired brain injury  
neuropsychiatric symptoms  
prevalence  
determinants  
nursing home  
long-term care

**Objectives:** Establishing the prevalence and determinants of neuropsychiatric symptoms (NPS) in patients with acquired brain injury (ABI) in nursing homes.

**Design:** Cross-sectional, observational study.

**Setting and Participants:** Patients 18–65 years old with ABI in special care units in Dutch nursing homes.

**Methods:** Nursing homes were recruited through the national expertise network for patients with severe ABI, regional brain injury teams, and by searching the Internet. Patient characteristics were collected through digital questionnaires. NPS were assessed with the Neuropsychiatric Inventory–Nursing Home version (NPI-NH) and the Cohen–Mansfield Agitation Inventory (CMAI), cognition with the Mini-Mental State Examination, and activities of daily living with the Disability Rating Scale. Psychotropic drug use (PDU) was retrieved from the electronic prescription system. Individual NPS were clustered. Associations between determinants and NPS were examined using multilevel multivariate linear regression models.

**Results:** In a population of 118 patients from 12 nursing homes, 73.7% had 1 or more clinically relevant NPS and 81.3% 1 or more agitated behaviors. The most common NPS were agitation, in particular aberrant motor behavior (24.6%), repetitious sentences/questions (35.5%), and constant requests for attention (34.6%), verbal (33.6%) and physical (50.5%) aggression, and irritability (28.0%). Male patients were more likely to display hyperactivity. Being married was associated with less verbally agitated behavior and pain was associated with a higher CMAI total score. PDU increased the likelihood of a higher NPI-NH total score.

**Conclusions and Implications:** NPS are common in patients with ABI ≤65 years of age residing in nursing homes. This is a first step to fill in the knowledge gap concerning NPS in this population. An increasing number of patients with severe ABI may survive the acute phase and will reside many years in nursing homes. It is important to shed more light on these NPS, with regard to course, magnitude, and severity, to ultimately develop appropriate care for this vulnerable group of patients.

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Little is known about neuropsychiatric symptoms (NPS) in the population of patients ≤65 years of age with severe acquired brain injury (ABI) residing in nursing homes. In our recent systematic review, we found 6 studies about NPS in patients younger than 65 years with ABI in long-term care.<sup>1</sup> Only 2 of these studies reported prevalence rates of psychotropic drug use (PDU). We found that NPS and PDU are common, in which depressive symptoms were the most reported NPS and tranquilizers the most prevalent psychotropic drugs. ABI has more often been studied in older patients living in nursing homes, mainly those with stroke and traumatic brain injury (TBI), which commonly

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reported higher prevalence rates of aggression and depression.<sup>2–4</sup> Higher prevalence rates of anxiety, however, were reported in stroke and lower in TBI.<sup>2,3</sup> In other settings, NPS in patients with ABI are common as well. In poststroke patients who were hospitalized, the most prevalent NPS were depression, irritability, and eating disturbances.<sup>5</sup> The most common NPS in patients with severe traumatic brain injury in rehabilitation programs were apathy and irritability.<sup>6</sup> Yet, little is known about determinants of NPS in ABI. Statistically significant associations have been found between aggression and gender, duration of admission, hypoxia as cause of ABI, impairment in activities of daily living, and the use of psychotropic medication.<sup>7–9</sup> Increasing levels of functional disability have shown a statistically significant association with NPS in patients with severe TBI.<sup>10</sup>

Patients with severe ABI who are unable to live at home are commonly admitted to long-term care facilities. Long-term care refers to health, social, and residential services given to chronically disabled persons over an extended period of time.<sup>11</sup> NPS are a common reason for admission. NPS put a high burden on patients, family, and nursing staff.<sup>12–14</sup> Behavioral changes may be related to lack of control, such as irritability and aggression, or lack of drive, such as apathy, reduced initiative, and poor motivation.<sup>15</sup> A recent review about experiences of giving and receiving care in TBI found that NPS, specifically verbal and physical aggression, hindered the provision of quality care and required the implementation of proactive nursing strategies to maintain safety for both patients with TBI and nurses.<sup>16</sup> Indeed, NPS may prompt prescription of psychotropic drugs. However, antipsychotics, prescribed for the treatment of psychosis, agitation, and aggression, may have adverse effects on cognition.<sup>17–19</sup> Also, uniformity in drug selection for the various NPS was shown to be limited, which was potentially due to the severity of the NPS and the lack of clinical practice guidelines.<sup>20</sup>

The total number of people with ABI and NPS in general is unknown. More insight into the prevalence and determinants of NPS is necessary to achieve appropriate use of psychotropic drugs and promote psychosocial interventions, in particular for patients with ABI  $\leq 65$  years of age in long-term care. Therefore, the aim of this study is to establish the (1) prevalence of NPS in general, and agitation/aggression in particular, and (2) the determinants of NPS among patients, with severe ABI being  $\leq 65$  years of age residing in Dutch nursing homes.

## Methods

### Study Design

This study is a cross-sectional, observational study among people 18–65 years of age with chronic ABI in Dutch nursing homes.

### Procedure

#### Recruitment nursing homes

Recruited nursing homes were to be visited by the first author and the research assistant for conducting the data collection. Professional care is provided in more than 480 long-term care organizations spread throughout the country.<sup>21</sup> To enhance logistical efficiency, nursing homes with ABI special care units for at least 10 patients were identified, contacted, and recruited. This was done through (1) the national expertise network for patients with severe ABI,<sup>22</sup> (2) the regional brain injury teams, (3) and the websites of nursing homes. In the Netherlands, 17 regional brain injury teams throughout the country provide information and advice about ABI to patients, family members, and professional caregivers.<sup>23</sup> Nursing homes that have participated in previous studies of our research group were contacted and recruited as well.<sup>24–26</sup> Nursing homes with ABI special care units were

contacted if their websites did not mention the size of their special care units.

### Residents

An e-mail was sent to the treating physicians of the identified nursing homes to inform them about the study and to ask them to systematically screen all residents  $\leq 65$  years of age in the chronic stage of ABI for inclusion. Inclusion criteria were (1) nursing home admission because of ABI; (2) being in the chronic phase of nonprogressive, stable forms of ABI such as TBI, stroke, and anoxia; (3) from 18 up to and including 65 years of age; and (4) residing in nursing homes for at least 4 weeks at the time of inclusion. The exclusion criteria were (1) being admitted for rehabilitation, temporary admission, or having outreaching nursing home care; (2) having prolonged disorders of consciousness like unresponsive wakefulness syndrome and minimally conscious state; and (3) being terminally ill at the time of inclusion defined as a life expectancy of less than 3 months.

### Assessment

The professional caregivers involved in the daily care of the residents observed symptoms during a 2-week period before assessment. After this period, these professional caregivers were visited by the first author or the research assistant for a structured interview administering the Neuropsychiatric Inventory–Nursing Home Version (NPI-NH; see below). Professional caregivers were also asked to fill in assessment instruments, the Cohen Mansfield Agitation Inventory (CMAI) and the Disability Rating Scale (DRS), through a web-based digital system. The treating physicians were asked to digitally register patient characteristics. Nursing home staff and the treating physicians were contacted by telephone if questionnaires were not returned, or if data they had provided were inconsistent, such as a date of injury that predates the date of birth.

### Patient Characteristics

The collected patient characteristics were gender, age, marital status, level of education, cause of ABI, age of onset ABI, duration of ABI, duration of nursing home admission, psychiatric history, pain, constipation, spasms, and the presence of PDU.

### Neuropsychiatric Symptoms

NPS were assessed with the Dutch version of the NPI-NH.<sup>27,28</sup> The NPI-NH is a structured interview administered to the patients' professional caregiver including 12 NPS: delusions, hallucinations, agitation, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor behavior, nighttime disturbances, and appetite/eating change. The frequency (F) and the severity (S) of each symptom are rated on a 4- and 3-point Likert-type scale. A score can be calculated for each symptom by multiplying the frequency and the severity resulting in values ranging from 0 to 12. An NPS is considered clinically relevant when the frequency  $\times$  severity score for an item is 4 or more. We grouped NPS based on a study in nursing home patients with mental and physical multimorbidity in which NPS were clustered after performing a factor analysis.<sup>29</sup> Irritability, agitation, and disinhibition were grouped in a cluster "hyperactivity"; depression, apathy, and anxiety in "mood/apathy"; and delusions and hallucinations in "psychosis."

Agitation and aggression were assessed using the Dutch version of the CMAI.<sup>30</sup> This instrument assesses 29 agitated or aggressive behaviors, which are scored on a 7-point frequency scale: 1 = never; 2 = less than once a week; 3 = 1–2 times a week; 4 = several times a week; 5 = 1–2 times a day; 6 = several times a day; and 7 = several times per hour. Individual behaviors were considered as clinically relevant when the behaviors appeared at least once a week or more

(frequency score of 3 or more).<sup>31</sup> The individual behaviors were grouped based on a study in institutionalized patients with dementia in the clusters “physically aggressive,” “physically nonaggressive,” and “verbally agitated.”<sup>32</sup>

### Disability

The Dutch version of the DRS was used to describe and assess ADL disabilities.<sup>33</sup> The DRS consists of 8 sections: eye opening, communication ability, motor response, feeding, toileting, grooming, level of functioning, and employability. Each item is rated on a 4-, 5-, or 6-point Likert-type scale. The total DRS score ranges between 0 and 29, a higher score representing a higher level of disability.

### Cognition

Cognitive functioning in general was assessed with the Dutch version of the Mini-Mental State Examination (MMSE) by the first author who gained experience during his 3-year older care specialist training program and in practice.<sup>34</sup> The MMSE includes 11 questions and measures orientation, attention, concentration, memory, language, and constructive capacity. The total score ranges from 0 to 30, and a lower score represents lower cognitive functioning. There is an inverse relationship between cognitive performance and age, and the median MMSE score is higher in people with longer duration of education.<sup>35</sup> Therefore, a score below 27 was considered to indicate cognitive impairment, which is recommended in people with higher educational levels.<sup>36,37</sup>

### Psychotropic Drug Use

The names, dosages, continuous and/or incidental usage, and prescription reasons of PDU were retrieved from the electronic prescription system. PDU was classified using the Anatomic Therapeutic Chemical (ATC) classification in anticonvulsants, antidepressants, antipsychotics, anxiolytics, and hypnotics.<sup>38</sup> The treating physicians were asked to register the indications for PDU (eg, depression, anxiety, epilepsy, or neuropathic pain) to determine if patients actually received psychotropic drugs because of NPS.

### Statistical analysis

Descriptive analyses were performed to describe the patient characteristics. Mean and standard deviation (SD) or median and interquartile ranges for continuous variables and frequencies for categorical characteristics were determined. The Wilson score interval was used to calculate 95% confidence intervals (95% CIs) for the prevalence of NPS.

With regard to determinants, we studied the association between the primary outcomes (1) the CMAI and NPI-NH total scores; (2) the cluster scores hyperactivity, mood/apathy, and psychosis from the NPI-NH; and (3) physically nonaggressive behavior, physically aggressive behavior, and verbally agitated behavior from the CMAI as dependent variables with the patient characteristics gender, age, marital status, level of education, cause of ABI, age of onset ABI, duration of ABI, duration of nursing home admission, psychiatric history, pain, constipation, spasms, disability, cognition, and the presence of PDU as independent variables. All dependent variables were used as continuous variables. The patient characteristics age, age of onset ABI, duration of ABI, duration of nursing home admission, disability, and cognition were used as continuous variables. Marital status was dichotomized in not married and married, level of education in none/low and secondary/high, and cause of ABI in TBI and non-TBI. The other characteristics were dichotomized in present and absent. Because of the hierarchical structure of our study, patients nested within nursing homes, we performed multilevel mixed model

analyses in which patients were only included if data of the outcomes and/or determinants were available. We used a model with a random intercept, and all other variables were fixed. Only determinants with at least 30 events in the subgroups were included in the analysis. A number of 30 representative participants from the population of interest has been suggested as a reasonable minimum recommendation for a study where the purpose is preliminary survey.<sup>39</sup> All determinants with a  $P < .20$ , which is often used to limit the possibility of missing determinants, from the multilevel univariate linear regression analysis were included in multilevel multivariate linear analyses to determine their unique effect on NPS.<sup>40</sup> We removed the least significant determinants stepwise until only significant determinants remained. Significance was defined as  $P < .05$  based on 2-sided testing.

According to literature, the prevalence rate of NPS in nursing homes is approximately 35%.<sup>41</sup> We assumed that 50% of the patients would meet the inclusion criteria and that the response rate would be 50%. Through the national expertise network for patients with severe ABI, the regional brain injury teams, and the nursing homes themselves, the number of patients residing on ABI special care units for at least 10 patients ( $n = 937$ ) was estimated. The expected population thus would approximately be 230 patients with ABI. A rule of thumb for a continuous outcome is that 1 determinant can be studied for every 10 patients.<sup>40,42</sup> With an estimated NPS prevalence rate of 35%, the number of patients with NPS would be 80 in a study population of 230 patients. The number of determinants that could be studied would then be 8. Statistical analyses were performed using SPSS, version 25.0 (IBM Corporation, Chicago, IL).

### Ethical approval

This study (case number 2017-3143) was presented in its entirety, including method of data collection and all used assessment instruments, for medical ethics review at the regional Committee on Research Involving Human Subjects (CMO) region Arnhem-Nijmegen, the Netherlands. The conclusion of the CMO was that it did not require ethical approval because our study did not involve scientific research according to the criteria of the Dutch Medical Research Involving Human Subjects Act and could be conducted without review by the CMO. The research project was performed according to the principles of the Declaration of Helsinki.<sup>43</sup> Patients were only included after written informed consent was provided by themselves or by the legal representative if the patient was not mentally competent. The questionnaires and assessment instruments were rendered anonymous.

### Results

Of the identified 28 nursing homes with ABI special care units with at least 10 patients, 12 nursing homes (42.9%) participated (Figure 1). In these nursing homes, a total of 245 out of 548 patients were eligible for inclusion and from these 245 patients informed consent was obtained in 118 patients, which is a response rate of 48.2%. Patient characteristics and PDU were missing in 1 patient, duration of ABI in 2 patients, and duration of nursing home admission in 1 patient. Data on the CMAI and MMSE was missing in 11 patients and DRS in 8 patients.

### Characteristics of the Patients

The male-female ratio was approximately 2:1. Cognitive impairment (MMSE score  $< 27$ ) was present in 72.9% of the patients (Table 1). The median DRS score was 8.50 with an interquartile range of 8, which represented moderately severe disabilities. The severity ranged from partially to extremely severe disabled. Eight patients were aphasic and 18 patients had physical disabilities not enabling them to perform actions such as taking and folding a piece of paper, writing, and drawing. Three patients were, according to the DRS, in a vegetative ( $n = 2$ ) or extremely vegetative state ( $n = 1$ ), also known as

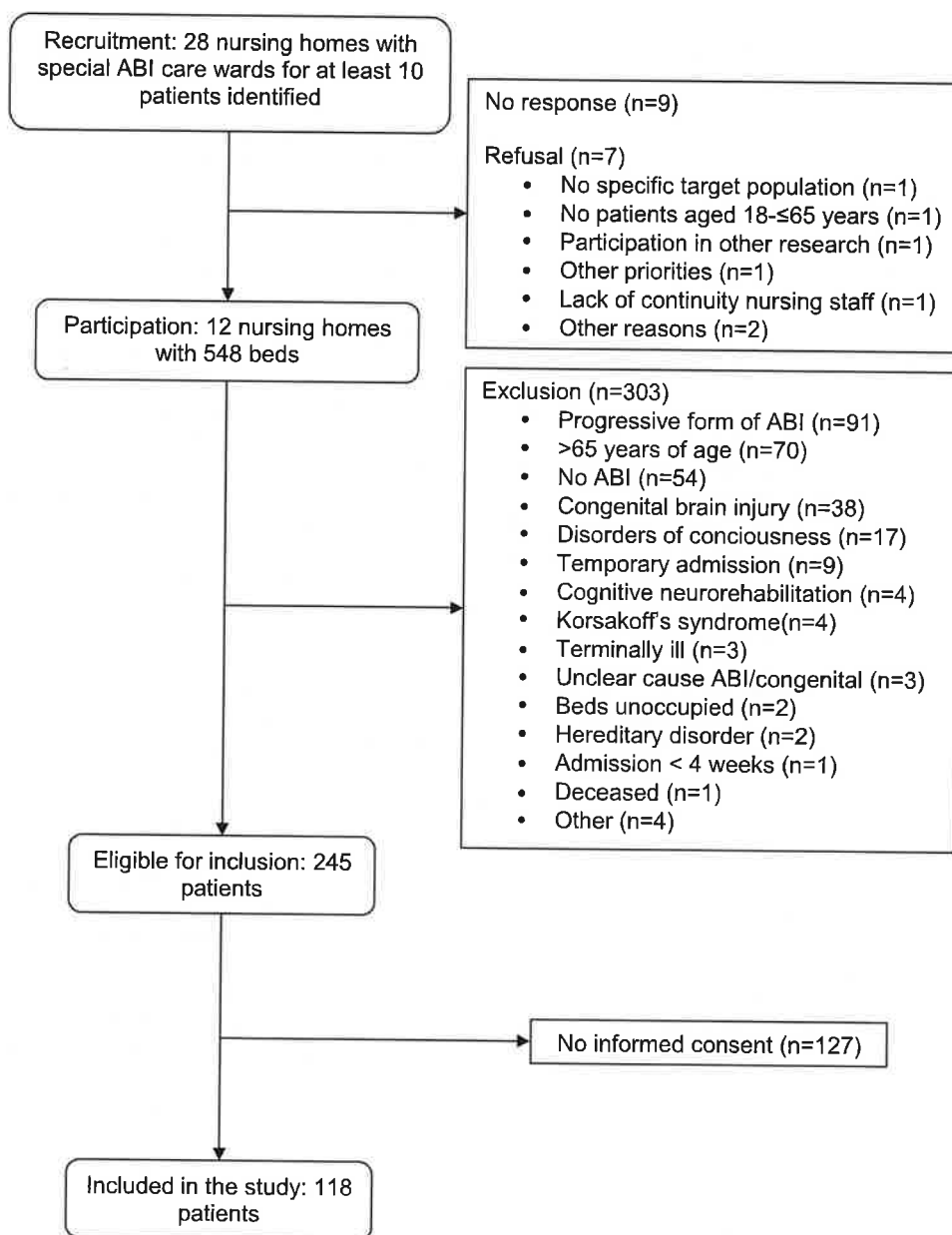


Fig. 1. Flow chart of the patient inclusion.

unresponsive wakefulness syndrome. Clinically, these patients appeared not to be in a vegetative state when visited by the first author. These scores are likely a reflection of their extremely severe disabilities.

#### Prevalence of NPS

Almost all patients (93.2%) had 1 or more NPS from the NPI-NH, whereas 73.7% of the patients had 1 or more clinically relevant NPS (Table 2). The most common clinically relevant NPS were agitation/aggression (30.5%), irritability (28.0%), and aberrant motor behavior (24.6%). Anxiety and depression were comorbid in 5.1% of the patients. Prevalence rates of the NPI-NH clusters hyperactivity, mood/apathy, and psychosis were 51.7%, 32.2%, and 9.3%, respectively.

According to the CMAI, 90.7% had 1 or more agitated behaviors, whereas 81.3% presented 1 or more clinically relevant agitated

behaviors (Table 2). The most common clinically relevant agitated behaviors were repetitious sentences/questions (35.5%), constant requests for attention (34.6%), and cursing or verbal aggression (33.6%). The prevalence rates of the clusters physically aggressive, physically nonaggressive and verbally agitated behaviors were respectively 50.5%, 44.9%, and 57.9%.

#### Determinants Associated With NPS

A total of 13 determinants could be studied in the multilevel linear univariate analyses. Constipation and spasms were excluded from the analyses because of fewer than 30 events. The number of determinants that could be included in the different multilevel multivariate linear analyses ranged from 3 to 9.

Male patients were more likely to display hyperactivity with a higher score of 3.39 (95% CI 0.70–6.08) compared with female patients.

Being married was associated with less verbally agitated behavior ( $-3.44$ , 95% CI  $-6.01, -0.88$ ) and pain was associated with a higher CMAI total score of 6.06 (95% CI 0.22–11.90). Patients with PDU had a higher score of hyperactivity of 3.75 (95% CI 1.23–6.27) and a higher NPI-NH total score of 11.83 (95% CI 6.59–17.07). All statistically significant determinants are listed in Table 3.

**Table 1**  
Characteristics of the Patients With ABI in Nursing Homes

Characteristics	Participants (n = 117)
Age, y, median (IQR; range)*	54.2 (12.9; 24.1–65.7)
Gender, n (%)	
Male	79 (67.5)
Female	38 (32.5)
Marital status, n (%)	
Single	64 (54.7)
Married	31 (26.5)
Divorced	19 (16.2)
Widow	3 (2.6)
Level of education, n (%)	
No education completed	4 (3.4)
Primary education	5 (4.3)
Secondary education	64 (54.7)
Higher professional education	10 (8.5)
University education	7 (6.0)
Other	3 (2.6)
Unknown	24 (20.5)
Cause of ABI, n (%)	
Traumatic	42 (35.9)
Nontraumatic	
Stroke	52 (44.4)
Anoxia	9 (7.7)
Post-brain tumour	5 (4.3)
Other	9 (7.7)
Age of onset ABI, y (n = 115), median (IQR; range)*	44.1 (19.3; 8–61)
Duration of ABI, y (n = 115), median (IQR; range)*	8.3 (14.4; 0.6–45.6)
Duration nursing home admission, y (n = 116), median (IQR; range)*	5.2 (7.1; 0.1–32.6)
Place of residence before admission, n (%)	
Rehabilitation center	33 (28.2)
Another nursing home	21 (17.9)
Mental health institution	17 (14.5)
Hospital	12 (10.3)
Rehabilitation unit in nursing home	10 (8.5)
Other	14 (12.1)
Unknown	10 (8.5)
Psychiatric history before ABI, n (%)	
No history	87 (74.4)
Substance abuse	14 (12.0)
Mood disorder	12 (10.3)
Personality disorder	6 (5.1)
Suicide attempt	3 (2.6)
Other	10 (8.5)
Comorbidity/complications, n (%)	
Pain	34 (29.1)
Spasms	23 (19.7)
Constipation	10 (8.5)
Delirium	1 (0.9)
MMSE score (n = 107), median (IQR; range)*	22 (12; 0–30)
Cognitive impairment (MMSE score <27)	78 (72.9)
DRS (n = 110), median (IQR; range)*	8.50 (8; 3–26)
Psychotropic drugs, n (%)	
Anticonvulsants	11 (9.4)
Antidepressants	33 (28.2)
Antipsychotics	29 (24.8)
Anxiolytics	28 (23.9)
Hypnotics	20 (17.1)

\*Non-normal distribution.

**Table 2**

The Prevalence Rates of the Clinically Relevant NPS in Patients With ABI in Nursing Homes Assessed by the NPI-NH and CMAI

Neuropsychiatric Symptoms	Frequency, n (%)	CI (%)
NPI-NH (n = 118)		
Delusions	9 (7.6)	3.8–14.4
Hallucinations	5 (4.2)	1.6–10.1
Agitation/aggression	36 (30.5)	22.6–39.8
Dysphoria/depression	18 (15.3)	9.5–23.3
Anxiety	12 (10.2)	5.6–17.4
Euphoria/elation	7 (5.9)	2.6–12.3
Apathy/indifference	21 (17.8)	11.6–26.2
Disinhibition	28 (23.7)	16.6–32.6
Irritability/lability	33 (28.0)	20.3–37.1
Aberrant motor behavior	29 (24.6)	17.3–33.5
Nighttime behavior disturbances	20 (16.9)	10.9–25.2
Appetite/eating disturbances	27 (22.9)	15.9–31.7
Hyperactivity	61 (51.7)	42.4–60.9
Mood/apathy	38 (32.2)	24.1–41.5
Psychosis	11 (9.3)	5.0–16.4
CMAI (n = 107)		
Pacing	20 (18.7)	12.1–27.6
Inappropriate robbing/disrobing	4 (3.7)	1.2–9.9
Spitting	7 (6.5)	2.9–13.5
Cursing or verbal aggression	36 (33.6)	25.0–43.5
Constant request for attention	37 (34.6)	25.8–44.5
Repetitious sentences/questions	38 (35.5)	26.7–45.4
Hitting	6 (5.6)	2.3–12.3
Kicking	5 (4.7)	1.7–11.1
Grabbing	12 (11.2)	6.2–19.1
Pushing	4 (3.7)	1.2–9.9
Throwing things	8 (7.5)	3.5–14.7
Making strange noises	21 (19.6)	12.8–28.7
Screaming	20 (18.7)	12.1–27.6
Biting	2 (1.9)	0.3–7.3
Scratching	5 (4.7)	1.7–11.1
Get to different place	10 (9.3)	4.8–16.9
Intentional falling	1 (0.9)	0.1–5.8
Complaining	34 (31.8)	23.3–41.6
Negativism	32 (29.9)	21.6–39.7
Eating inappropriate substances	1 (0.9)	0.1–5.8
Hurting oneself or others	2 (1.9)	0.3–7.3
Handling things inappropriately	4 (3.7)	1.2–9.9
Hiding things	10 (9.3)	4.8–16.9
Hoarding things	10 (9.3)	4.8–16.9
Tearing things	3 (2.8)	0.7–8.6
Performing repetitious mannerisms	21 (19.6)	12.8–28.7
Verbal sexual advances	11 (10.3)	5.5–18.0
Physical sexual advances	5 (4.7)	1.7–11.1
General restlessness	34 (31.8)	23.3–41.6
Physically aggressive behavior	54 (50.5)	40.7–60.2
Physically nonaggressive behavior	48 (44.9)	35.3–54.8
Verbally agitated behavior	62 (57.9)	48.0–67.3

## Discussion

This is the first study that extensively investigated NPS in patients with ABI  $\leq 65$  years of age in Dutch nursing homes. In a population of 118 patients from 12 nursing homes, the most common clinically relevant NPS were agitation, in particular aberrant motor behavior, repetitious sentences/questions, and constant requests for attention, verbal and physical aggression, and irritability. Gender, marital status, pain, presence of PDU, disability, and cognition were statistically significant determinants of NPS.

In line with previous studies conducted in nursing homes, we found comparable prevalence rates of dysphoria/depression.<sup>44–47</sup> The prevalence of anxiety was similar compared to an American nursing home population of 239 patients with TBI.<sup>45</sup> We found, however, more NPS and physical aggression compared with other studies in nursing home patients with TBI and ABI.<sup>41,44,48</sup> With regard to other settings, we found less depression, irritability, eating disturbances, apathy,

**Table 3**  
The Results (Coefficient and Confidence Intervals) From the Multilevel Multivariate Linear Regression Analysis

Independent Variables*	NPI-NH			
	Hyperactivity	Mood/Apathy	Psychosis	Total Score
Gender (male)	3.39 (0.70, 6.08)	—	—	—
Presence of PDU	3.75 (1.23, 6.27)	2.65 (0.81, 4.49)	1.81 (0.79, 2.82)	11.83 (6.59, 17.07)
DRS	—	0.20 (0.02, 0.39)	—	0.62 (0.09, 1.15)
	CMAI			
	Physically Aggressive	Physically Nonaggressive	Verbally Agitated	Total Score
Marital status (married)	—	—	−3.44 (−6.01, −0.88)	—
Cause of ABI (non-TBI)	—	−2.04 (−4.01, −0.08)	—	—
Age of onset ABI	−0.11 (−0.18, −0.04)	—	—	−0.39 (−0.60, −0.18)
Presence of psychiatric history	—	2.91 (0.74, 5.08)	—	—
Presence of pain	—	—	—	6.06 (0.22, 11.90)
Presence of PDU	2.12 (0.29, 3.94)	—	—	—
MMSE	—	—	0.17 (0.04, 0.29)	—
DRS	0.26 (0.07, 0.44)	—	—	—

\*Nonsignificant results were omitted.

anxiety, and disinhibition in comparison with hospitalized patients with stroke and patients with severe TBI in rehabilitation programs.<sup>5,6</sup> Besides that, we found more agitation. Possible explanations for differences in prevalence rates are different populations, specifically ABI vs TBI and hospital vs nursing home, and the use of different instruments.

In contrast to other studies that found a relationship between psychiatric comorbidity, such as premorbid alcohol abuse and depression, and aggression, we did not find these associations.<sup>10,49,50</sup> We found an association between PDU and more physical aggression. According to a study of 152 patients admitted to a postacute residential brain injury rehabilitation program, the use of psychotropic medication increased the odds of verbal and physical aggression in a subset of 77 patients.<sup>9</sup> PDU was also associated with more hyperactivity. The prescription of PDU is probably higher because of the problematic nature of the behavior caused by a lack of control. Furthermore, we found that patients with ABI who were not married were more likely to be (verbally) agitated than patients who were married. Higher agitation may be related to unmarried people with NPS being more prone to nursing home admission than married people. This is implicated by the study of 7219 patients with TBI predicting institutionalization after inpatient rehabilitation showing that people who lived alone before injury were more likely to be discharged to an institutional setting.<sup>51</sup>

Besides the statistically significant differences in outcome, clinical relevance is important as well. Because neither the observed difference nor its statistical significance may indicate clinical significance, the minimal clinically important difference has been suggested as a more useful measure of effectiveness.<sup>52</sup> For instance, one study adopted a value of 8 points change in total score on the NPI as a minimum clinically important difference in patients with Alzheimer's disease.<sup>52</sup> According to another study, a change of 11 points on the NPI-NH and 8 points on the CMAI total scores can be considered as a true behavioral change in patients with dementia.<sup>53</sup> However, minimal clinically important differences in patients with ABI are unknown and will probably be different.

#### Strengths and Limitations

Strengths of this study are that NPS have been studied extensively in patients with ABI using a variety of assessment instruments for the first time in a substantial number of Dutch nursing homes spread throughout the country, the use of strict inclusion and exclusion criteria, and a high response rate of nurses and treating physicians in

the participating nursing homes. However, there are some considerations about the measurement instruments and possible limitations to address. NPS were assessed with 2 instruments. We found some differences in prevalence rates between NPI-NH and CMAI, which could be explained by the CMAI only measuring frequencies and the NPI-NH combining frequency and severity scores. According to the DRS, 3 patients were in a vegetative or extremely vegetative state, but not clinically when visited by the first author. This may be caused by a floor effect of the DRS. A limitation is the low response rate of patients. The CMAI is not validated for use in ABI, but it gives a rich description of individual aggressive behavior and does not require training. Furthermore, the CMAI has been validated in the assessment of behavioral disorders in older nursing home patients.<sup>30,54</sup> Use of extensive language in the MMSE might lead to unreliable results in aphasic patients and patients who do not speak the Dutch language.<sup>55</sup> Eight patients were aphasic and assessing cognition was not possible in 5 of these patients. These 5 patients were excluded from the analysis with regard to the MMSE. Physical disabilities in patients with ABI, such as paralysis, might have led to an underestimation of their cognitive abilities because of not being able to perform actions such as taking and folding a piece of paper, writing, and drawing.

The reason for the low participation rate of nursing homes was mainly unknown because of the nonresponse of nursing homes. In a small number of cases, reasons were the absence of patients with ABI with regard to age and inclusion criteria, lack of continuity in nursing staff, already involved in other studies, or having other priorities. These reasons were reported by the nursing homes during recruitment. The low rate of informed consent may be due to not speaking the Dutch language, leading to selection bias. The low sample size and small number of nursing homes might limit the generalizability. Another limitation is that there was no even distribution of patients between the participating nursing homes. Almost a quarter of the patients were recruited from 1 nursing home.

#### Recommendations

The results of this study could give direction to the kind of care that is needed for patients with ABI  $\leq 65$  years of age residing in nursing homes. More insight into the magnitude and severity of NPS, however, is needed to enhance the provision of quality care by, for example, improving nursing home staff's skills, through education, to improve managing NPS. Provision of care is facilitated by general care standards that have been developed in the Netherlands for patients with ABI to guide the treatment of consequences, in particular NPS.<sup>56–58</sup>

Recommendations for future studies can therefore be made, such as more prevalence studies about NPS in ABI with greater sample sizes and validated assessment instruments for agitation/aggression to enhance the generalizability of findings. We also recommend conducting longitudinal studies to determine the course of NPS in patients with ABI residing in nursing homes. Furthermore, we advise to determine the minimum clinically important differences in total scores to assess the clinical relevance of determinants in this population of patients.

## Conclusions and Implications

NPS are common in patients with ABI  $\leq 65$  years of age residing in nursing homes. This is a first step to fill in the knowledge gap concerning NPS in this population of patients as concluded in our systematic review. An increasing number of patients with severe ABI may survive the acute phase of ABI as a result of modern medicine, and in contrast to older people, they will reside many years in nursing homes. It is important to shed more light on these NPS, with regard to course, magnitude, and severity, to ultimately develop appropriate care for this vulnerable group of patients.

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