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Personality traits and course of symptoms of depression and apathy after stroke: Results of the CASPER study

Elles Douven[a], Julie Staals[b], Syenna H.J. Schievink[a], Robert J. van Oostenbrugge[b], Frans R.J. Verhey[a], Sascha Wetzels-Meertens[c], Sebastian Köhler[a], Pauline Aalten[a,*]

[a] Alzheimer Center Limburg and School for Mental Health and Neuroscience (MHeNs), Department of Psychiatry and Neuropsychology, Maastricht University, Maastricht, the Netherlands
[b] Cardiovascular Research Institute Maastricht (CARIM), Department of Neurology, Maastricht University Medical Center (MUMC+), Maastricht, the Netherlands
[c] Maastricht University, Maastricht, the Netherlands

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ABSTRACT

Objective: Post-stroke depression (PSD) and post-stroke apathy (PSA) are both associated with adverse outcome after stroke. This study aimed to examine whether personality traits predict the course of PSD and PSA.
Methods: In this prospective cohort study, 240 stroke patients completed the NEO Five Factor Inventory, Montgomery-Åsberg Depression Rating Scale, and Apathy Evaluation Scale at 3 months post-stroke. Neuropsychiatric assessment was repeated at 6- and 12-month follow-up after initial testing.
Results: Linear mixed models showed that high neuroticism scores were associated with higher depression levels at baseline, and this association remained stable at follow-up. High extraversion scores and high conscientiousness scores were associated with lower apathy levels at baseline. For neuroticism, a significant interaction with time was found, with higher neuroticism scores at baseline being associated with an increase in apathy scores from 6-month to 12-month follow-up. Prospective analyses showed that high extraversion predicted low apathy levels at 6-month and 12-month follow-up independent of its relations with baseline depression and apathy. High neuroticism predicted high apathy levels at 12-month follow-up, whereas high agreeableness and high openness predicted high apathy levels and low apathy levels, respectively, at 6-month follow-up. None of the personality traits predicted depression scores at follow-up.
Conclusion: Personality traits are associated with the development and sustainability of PSD and PSA. The traits associated with PSD and PSA were different, providing support for the independence of these constructs. The findings highlight the importance to take personality traits into account as a potential vulnerability factor for PSD and PSA.

1. Introduction

Apathy and depression are common neuropsychiatric consequences after stroke, both showing prevalence rates of around 30% [1,2]. Apathy can be defined as a disorder of motivation, characterized by diminished goal-directed behavior and cognitive activity and emotional indifference [3]. Post-stroke apathy (PSA) and post-stroke depression (PSD) frequently co-occur and there is considerable overlap in symptoms between them, particularly in the key criterion "loss of interest" [4]. However, PSA also frequently develops independent from PSD, and a meta-analysis showed that in 60% of PSA patients apathy developed in absence of a depressed mood [2]. Differentiation between PSD and PSA and timely recognition is however important, as it has been suggested that PSD and PSA may benefit from different treatment strategies [5] and both syndromes are associated with adverse outcome [6–8] and reduced quality of life after stroke [2,9–11]. Despite the similarities between PSD and PSA, several studies found also evidence for differences in associated factors for PSD and PSA. From a biological perspective, PSD and PSA have been linked to different lesion characteristics [12]. Also, damage to microstructural white matter networks has been linked to both PSA and PSD [13,14], although it remains to be studied whether both are associated with damage to different subnetworks. Other studies found evidence that different monoaminergic neuroanatomic pathways are associated with PSD and PSA, with serotonergic pathways being more associated with depression and dopaminergic pathways being more associated with apathy [15–18]. However, additional studies are needed to examine the role of monoamine dysregulations in PSA and PSD. While previous research on

* Corresponding author at: School for Mental Health and Neuroscience, Maastricht University, P.O. BOX 616 (DRT12), 6200 MD Maastricht, the Netherlands.
E-mail address: p.aalten@maastrichtuniversity.nl (P. Aalten).

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determinants of PSD and PSA focused mainly on stroke-related factors, such as lesion characteristics [12,19–21], psychological factors, including personality traits, may play a role as well.

Personality traits are relatively stable manners of feeling, thinking, and acting of individuals [22] and according to the five-factor model [23], personality can be represented by a five-factor trait structure, comprising neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. Previous studies in the general population found personality traits, and particularly neuroticism, to be an important predictor of onset and course of neuropsychiatric symptoms [24–27], but studies on personality factors in a stroke population are scarce. Some previous cross-sectional studies have reported an association between neuroticism and PSD [28,29], particularly in the acute stroke phase [29,30]. Only a single prospective study has examined the influence of personality traits on the development of PSD and this study showed that high neuroticism was an important predictor of 1-year PSD [31], but no evidence was found for associations with any of the other five-factor personality traits. For PSA, the relationship with personality traits has only been examined in one study, but no association was found [32].

Information on personality could be helpful to detect patients at risk for developing neuropsychiatric symptoms in patients recovering from stroke. Previous cross-sectional studies already indicated a strong link between neuroticism and PSD. However, as previously pointed out by Aben et al. [31], the association between personality traits and neuropsychiatric symptoms after stroke should preferably be studied in large longitudinal cohorts with multiple time points, assessing all five-factor personality. PSD and PSA are independent though overlapping syndromes [33,34], and the studies examining personality traits in association with PSD did not control for this overlap in symptomatology between the two syndromes, which could have biased the results. Therefore, the present study followed a cohort of 250 stroke patients to assess whether personality traits are predictive for the development and course of PSD and PSA over 12 months.

2. Methods

2.1. Study population

Participants were enrolled in the Cognition and Affect - a Prospective Evaluation of Risks (CASPER) study, a prospective clinical cohort study into predictors of cognitive and neuropsychiatric disorders after stroke. The study was approved by the Medical Ethics Committee of Maastricht University Medical Center (MUMC+).

We included patients who suffered from a non-fatal ischemic or hemorrhagic stroke who were admitted to the Stroke Unit of MUMC+ or Zuyderland Medical Center in Sittard and Heerlen (The Netherlands) between June 2013 and August 2015. Stroke was defined as a clinical stroke syndrome, with sudden neurological dysfunction lasting > 24 h, with no apparent cause other than that of vascular origin. Ischemic strokes could be cortical or lacunar, and hemorrhagic strokes were non-traumatic deep, lobar, cerebellar, or brainstem hemorrhages as evidenced by a clinical brain scan (for details see Douven et al. [35]). Exclusion criteria include age < 40 years, pre-stroke dementia, pre-existing cognitive impairment, intellectual disability, a Mini-Mental State Examination Score < 15 [36], neurological or psychiatric diseases other than depression that are known to affect cognition, insufficient knowledge of the Dutch language, too severe aphasia to understand the study procedure, an Informant Questionnaire on Cognitive Decline in the Elderly score ≥ 3.60 [37], no written informed consent, blindness, history of stroke < 3 years or residual symptoms from previous stroke, and post-surgery stroke / post-anoxic encephalopathy.

2.2. Procedure

Baseline measurements (T0) were scheduled approximately 3 months after stroke (median = 2.9 months, interquartile range = 2.0–4.3), to avoid interference with acute care and rehabilitation. Socio-demographic characteristics were recorded, and neuropsychiatric questionnaires were administered to the patient, in which the presence of depression and apathy was assessed. The neuropsychiatric interview was repeated in the chronic stroke phase (9 and 15 months post-stroke; T1 and T2, respectively). Personality was only assessed at T0, as it was assumed that personality traits remain stable over time.

2.3. Clinical measures

Personality was assessed with the NEO Five-Factor Inventory (NEO-FFI) [38,39]. This self-report questionnaire consists of 60 statements covering the 5 personality traits extraversion, neuroticism, openness to new experiences, agreeableness, and conscientiousness. Each statement was rated by the participant on a 5-point scale ranging from “strongly disagree” to “strongly agree”. For each personality trait a total dimension score between 12 and 60 was obtained. A median split was applied on all personality domains to dichotomize the personality traits in low versus high personality domains [40].

The severity of PSD symptoms was measured with the Montgomery-Åsberg Depression Rating Scale (MADRS), a 10-item clinician-rated scale designed to be especially sensitive to change in symptom severity [41]. Each item was scored from 0 to 6, resulting in a total score between 0 and 60, with higher scores reflecting more severe symptoms of depression. The MADRS was used as outcome measure of PSD symptoms as it focuses less on somatic symptoms, and is therefore evaluated as a valid instrument for measuring the severity of depressive symptoms after stroke [42]. In addition, the Mini International Neuropsychiatric Inventory (MINI), a semi-structured interview based on DSM-IV criteria, was administered for the diagnosis major depressive disorder (MDD) or minor depression (MIND) by a trained research (neuro)psychologist [43].

The Apathy Evaluation Scale (AES) was used to measure the presence and severity of PSA [44]. Example items from the AES are: “*S/he gets things done during the day”, “When something good happens, s/he gets excited” and “S/he has initiative”*. In total, there are 18 items which are rated on a 4-point scale, resulting in a total score between 18 and 72, with higher scores representing a higher level of apathy symptoms. The clinician-rated version of the AES was used, as this questionnaire is the best available and a frequently used instrument for measuring apathy in stroke patients [45]. A cut-off score of ≥37 can be applied to define clinically relevant apathy [33,46].

The Barthel Index [47] was used as a measure of impairment in activities of daily living.

2.4. Statistical analysis

All statistical analyses were performed with Stata version 13.1 for Mac OS X (StataCorp LP, College Station, TX, USA). An alpha level of .05 (two-sided) was used for all analyses. Differences in demographic variables between patients who completed all measurements and patients who dropped out at 1 or 2 time points were tested using χ^2 tests for qualitative variables and *t*-tests for quantitative variables. Separate linear mixed models were performed to measure the effect of personality traits on the course of depression (MADRS score) or apathy (AES-C score) from T0 to T2 as outcome measure. The models included a random intercept and random slope with an unstructured correlation matrix as this resulted in the best fit according to likelihood ratio testing. The analyses were corrected for age, sex, highest level of education, history of depression, and Barthel Index score, as based on previous studies these factors seem to influence the association between personality traits and PSD [31], and probably also PSA. Additionally, we also added apathy score to the model to correct for a possible confounding effect of apathy on depression, and vice versa, because of a

possible overlap in symptomatology. In a sensitivity analysis, a group (personality trait: low, high) by time (3-levels: T0, T1, T2) interaction was included to study differences in the course of depression or apathy between the groups. Prospective analyses were performed to examine whether personality traits were predictive for depressive or apathetic symptoms at follow-up in a linear regression analysis. Furthermore, in additional sensitivity analyses we examined the role of stroke category (i.e. cortical ischemic, lacunar ischemic, hemorrhagic stroke) and the influence of baseline psychopathology.

3. Results

Of the 619 eligible patients, 250 (40.4%) patients agreed to participate and signed informed consent. Refusers were more often female (53.4% versus 35.6%; $\chi^2 = 18.971$, $df = 1$, $p < 0.001$) and older than participants (73.2 ± 12.3 versus 67.3 ± 11.8 years, $t(617) = 5.983$, $p < 0.001$). Of the 250 participants, 241 (96%) completed the NEO-FFI. One patient was excluded because the responses given on questionnaires were considered unreliable, resulting in a total of 240 patients. Of them, 211 (87.9%) completed T1 (Supplementary Fig. 1). Twelve patients dropped-out at T2 (10 refused, 2 deceased) and eighteen of the patients who did not participate at T1 re-entered the study at T2, which resulted in 217 (89.7%) patients who completed T2. No differences were found between the 22 patients (9.1%) that missed 1 or 2 time points and the 219 patients (90.4%) who completed all measurements (Supplementary Table 1).

Table 1 shows the baseline characteristics of the total sample. At T0, 26 patients (10.8%) met DSM-IV criteria for either MDD (n = 13) or MIND (n = 13). A MINI depression diagnosis (MDD or MIND) was found in 14.2% at T1, and in 11.1% at T2. The average MADRS score at T0 was 6.1 ($SD = 5.8$) in the total sample, 15.9 ($SD = 7.4$) in patients with a MINI depression diagnosis and 4.9 ($SD = 4.3$) for non-depressed patients ($F = 121.5$, $p < 0.001$). Mean MADRS scores in the total cohort remained stable at T1 (6.8, $SD = 7.2$) and T2 (6.6, $SD = 7.5$). Average AES-C scores were 26.4 ($SD = 7.9$) at T0, 28.4 ($SD = 9.0$) at T1 and 28.1 ($SD = 9.4$) at T2. Twenty-four patients (10.0%) scored above the cutoff on the AES-C at T0. This frequency increased to 19.9% at T1 and decreased to 16.7% at T2.

Table 1
Baseline characteristics of patients.

Variable	Total (n = 240)
Age in years (SD)	67.31 (11.80)
Male sex, n (%)	157 (65.4)
Low education, n (%)	97 (40.6)
Middle education, n (%)	84 (35.2)
High education, n (%)	58 (24.3)
First-ever stroke, n (%)	224 (93.3)
Barthel score (SD)	19.47 (1.45)
Personality score (SD)	
Neuroticism	31.63 (4.87)
Agreeableness	36.53 (4.61)
Openness	36.83 (4.09)
Extraversion	38.23 (4.19)
Conscientiousness	39.63 (3.76)
History of depression, n (%)	55 (22.9)
Family history of depression, n (%)	34 (14.2)
MADRS score (SD)	6.06 (5.84)
AES-C score (SD)	26.41 (7.88)
MINI minor/major depression, n (%)	26 (10.8)
MDD, n (%)	13 (5.4)
MIND, n (%)	13 (5.4)
PSA, n (%)	24 (10.0)

AES-C, Apathy Evaluation Scale Clinician-rated; MADRS, Montgomery-Åsberg Depression Rating Scale; MDD, major depressive disorder; MIND, minor depression. PSA, post-stroke apathy.

3.1. Personality traits and post-stroke depressive symptoms

Linear mixed models were performed examining the relationship between personality scores and depression scores over time. For neuroticism, higher neuroticism scores were associated with higher depression scores at baseline ($\chi^2 = 15.88$; $df = 1$; $p < .001$). No significant interaction with time was found. With respect to the other personality traits, no significant results were found for agreeableness, openness, extraversion, or conscientiousness, respectively (Table 2).

A sensitivity analysis was performed to examine group-by-time interactions with linear mixed models examining differences in the course of depression levels for patients scoring high or low on the personality traits based on dichotomization. The results showed that significantly higher depression scores were found at T0 in patients with high neuroticism ($\chi^2 = 13.31$; $df = 1$; $p < 0.001$). This group effect remained significant at T1 ($p = 0.011$) and T2 ($p = 0.002$; Fig. 1). No significant group difference in depression score was found at T0 between patients with high and low scores on agreeableness, openness, extraversion, or conscientiousness, respectively. None of the personality traits showed a significant overall group-by-time interaction. Also, no significant change between individual time points (baseline to T1, or baseline to T2) was found, implying there were no significant differences in the course of depressive symptoms over time (see Supplementary Table 2).

3.2. Personality traits and post-stroke apathy symptoms

Linear mixed models examining the relationship between personality scores and apathy scores over time showed that higher extraversion ($\chi^2 = 31.93$; $df = 1$; $p < .001$) and higher conscientiousness ($\chi^2 = 4.30$; $df = 1$; $p = .038$) scores were associated with lower apathy scores at baseline. For neuroticism, a significant interaction with time was found, and time-stratified analyses showed that higher neuroticism scores at baseline were associated with an increase in apathy scores from T0 to T2 ($\chi^2 = 4.90$; $df = 1$; $p = .027$).

A sensitivity analysis was performed to examine group-by-time interactions with linear mixed models examining differences in the course of apathy levels for patients scoring high or low on the personality traits based on dichotomization. The results showed that significantly higher apathy scores were found in patients with low extraversion at T0 ($\chi^2 = 25.66$; $df = 1$; $p < 0.001$), which remained stable at T1 ($p < 0.001$; Fig. 2A) and T2 ($p < 0.001$). Apathy scores were almost significantly higher in patients with low openness at T0 ($\chi^2 = 3.83$; $df = 1$; $p = 0.050$), which became significant at T1 ($p = 0.010$, Fig. 2B), but not at T2. Similarly, significantly higher apathy scores were found in patients with low conscientiousness at T0 ($\chi^2 = 5.08$; $df = 1$; $p = 0.024$), which remained stable at T1 ($p = 0.016$), but not at T2 (Fig. 2C). With respect to neuroticism and agreeableness, no significant group difference in apathy score was found at T0. None of the personality traits showed a significant overall group-by-time interaction. Also, no significant change between individual time points (baseline to T1, or baseline to T2) was found, implying there were no significant differences in change of apathy over time (see Supplementary Table 2).

3.3. Prospective analyses

Linear regression analyses were conducted to examine whether personality traits were predictive for depressive or apathetic symptoms at follow-up independent of baseline associations with depression and apathy. MADRS or AES-C scores at 6 or 12-month follow-up were included as outcome measure and personality trait as predictor, and the analyses were corrected for age, sex, highest level of education, history of depression, Barthel Index score, and baseline depression and apathy scores to partial out the effect of concomitant psychopathology. Controlling for depression and apathy levels at baseline, none of the personality traits were associated with depression scores at T1 or T2,

Table 2
Differences in baseline depression and apathy and change in depression and apathy by continuous personality trait score.

Parameter	Time						
	Baseline		Change T0–T1		Change T0–T2		Personality by time[c]
	Difference	95% CI	Change	95% CI	Change	95% CI	χ^2 (df = 2)
MADRS score by							
Neuroticism	0.27[b]	0.14, 0.40	−0.03	−0.18, 0.13	0.10	−0.07, 0.27	2.34
Agreeableness	0.07	−0.08, 0.21	0.09	−0.08, 0.25	0.16	−0.02, 0.35	3.10
Openness	−0.12	−0.28, 0.04	0.01	−0.18, 0.20	0.04	−0.16, 0.25	0.19
Extraversion	−0.02	−0.18, 0.14	0.04	−0.14, 0.22	−0.07	−0.27, 0.13	1.34
Conscientiousness	0.12	−0.05, 0.29	−0.09	−0.29, 0.11	0.08	−0.14, 0.30	2.59
AES-C score by							
Neuroticism	0.05	−0.14, 0.25	0.14	−0.04, 0.32	0.24[a]	0.03, 0.45	5.01
Agreeableness	0.13	−0.07, 0.34	0.07	−0.12, 0.26	−0.09	−0.32, 0.14	2.44
Openness	−0.20	−0.43, 0.02	−0.09	−0.31, 0.13	−0.07	−0.33, 0.18	0.63
Extraversion	−0.60[b]	−0.81, −0.39	−0.04	−0.25, 0.17	0.02	−0.23, 0.27	0.36
Conscientiousness	−0.26[a]	−0.50, −0.01	0.04	−0.20, 0.27	−0.10	−0.38, 0.17	1.36

Model: personality trait, time, personality by time, sex, age at baseline, education, Barthel score at baseline, and history of depression. Analyses with MADRS score as outcome were additionally corrected for AES-C score, and vice versa. AES-C, Apathy Evaluation Scale Clinician-rated; CI, confidence interval; MADRS, Montgomery-Åsberg Depression Rating Scale.

[a] $p < 0.05$.

[b] $p < 0.01$.

[c] Overall interaction between personality trait and time (baseline, 6-month follow-up, 12-month follow-up, as indicated by χ^2, df = 2).

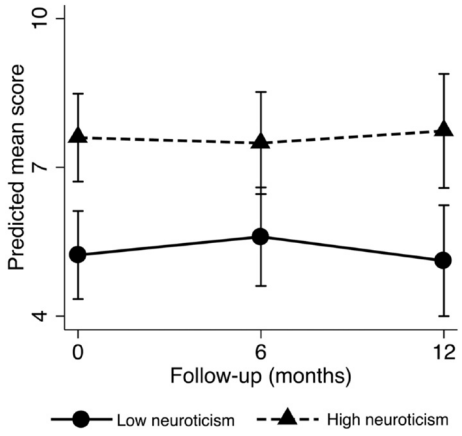

Fig. 1. Course of depressive symptoms by neuroticism group.
Based on random-effects analysis with random intercept, random slope and unstructured correlation matrix, adjusted for age at baseline, sex, level of education, Barthel Index, history of depression, and apathy score. Predicted mean scores are estimated marginal means for neuroticism group by time, with all covariates fixed at their means. Higher mean scores indicate a higher level of depression.

but high neuroticism was a significant predictor of high apathy scores at T2 (B = 2.48, p = .028), but not at T1 (B = 1.02, p = .308). High agreeableness was a significant predictor of high apathy scores at T1 (B = 2.25, p = .019), but not at T2 (B = 1.28, p = .263). High openness was a significant predictor of low apathy scores at T1 (B = −2.07, p = .028), but not at T2 (B = −1.02, p = .362). High extraversion was a significant predictor of lower apathy scores at T1 (B = −2.13, p = .031), and at T2 (B = −2.91, p = .011), while high conscientiousness was neither associated with apathy scores at T1, nor with apathy scores at T2.

3.4. Additional sensitivity analyses

To examine if stroke category might be of influence on the relationship between PSD, PSA and personality, the main analyses were repeated with stroke category (i.e. non-lacunar ischemic, lacunar ischemic, hemorrhagic stroke) added as a covariate in a sensitivity analysis (see Supplementary Table 3). The inclusion of stroke category as covariate in the analyses did not change the results.

Another sensitivity analysis was performed to examine whether the results may be confounded by the psychopathological symptoms present at baseline. The exclusion of patients with a minor or major depressive disorder at baseline (n = 26), based on the MINI, did not change the association between personality traits and depressive symptoms (see Supplementary Table 4). For apathy, the exclusion of patients with an AES-C score ≥ 37 at baseline (n = 24) changed the results to some extent for the personality traits neuroticism, openness, and conscientiousness. A significant overall interaction was found between neuroticism and time (χ^2 = 6.28; df = 2; p = .043). Time-stratified analyses showed a significant increase in apathy scores from T0 to T1 (χ^2 = 5.38; df = 1; p = .020) and from T0 to T2 (χ^2 = 4.13; df = 1; p = .042) in patients scoring high on neuroticism. For openness and conscientiousness, no significant group difference in apathy score was found at T0 between patients with high and low scores on openness or conscientiousness and no significant differences were found in the course of apathy symptoms over time (group-by-time interactions).

4. Discussion

This study investigated whether personality traits are a predictive factor for the development and course of depressive or apathetic symptoms after stroke. The main finding of this study was a consistent positive relationship between PSD and neuroticism over the course of 12 months, whereas there was a consistent negative relationship between PSA and extraversion. Furthermore, a negative association between PSA and openness and conscientiousness was found at baseline and 6-month follow-up, but not at 12-month follow-up. None of the personality traits showed a significant overall group-by-time interaction.

Our finding that individuals who score high on neuroticism are more likely to develop depressive symptoms post-stroke is in agreement with the results of the 1-year longitudinal study of Aben et al. [31] and the cross-sectional study of Hwang et al. [28]. In contrast with earlier studies on neuroticism and depression [28,31], we also controlled for level of apathy, as it might influence this relationship. Research has shown that social inhibition [48] and maladaptive forms of emotion regulation [49], which may both be associated with apathy [50,51], mediate the relationship between neuroticism and depression in

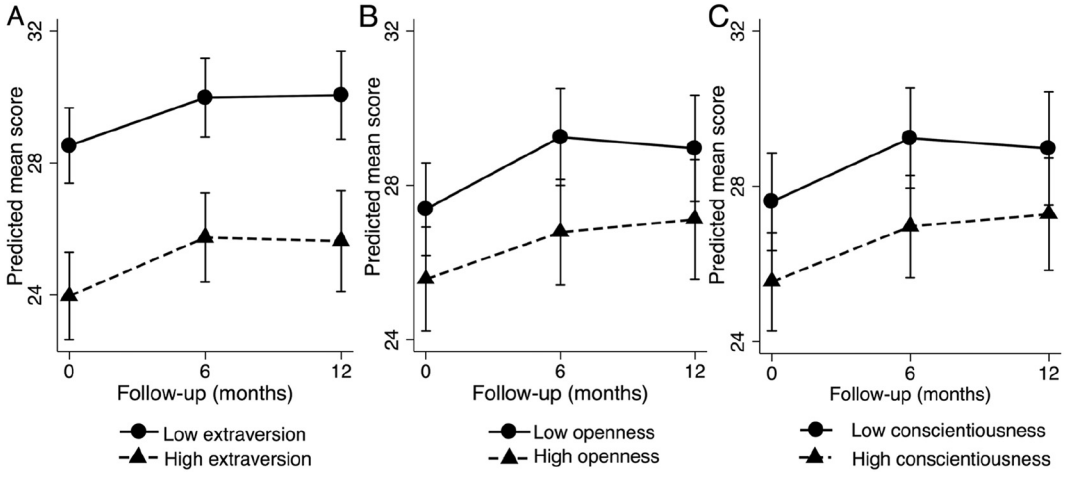

Fig. 2. Course of apathy by extraversion, openness, and conscientiousness group.
A, course of apathy scores by extraversion group. B, course of apathy scores by openness group. C, course of apathy scores by conscientiousness group. Based on random-effects analysis with random intercept, random slope and unstructured correlation matrix, adjusted for age at baseline, sex, level of education, Barthel Index, history of depression, and depression score. Predicted mean scores are estimated marginal means for personality trait group by time, with all covariates fixed at their means. Higher mean scores indicate a higher level of apathy.

elderly. Emotion regulatory processes can be affected by stroke, which can have a negative influence on social participation [52]. Therefore, also in stroke patients it may be of importance to look at the specific effect of neuroticism on PSD, independent of PSA. In contrast to our findings, Van Mierlo et al. [52] reported that extraversion was associated with PSD at 2 months post-stroke, too, which might be explained by the fact that they did not consider the role of PSA in this association.

For PSA, individuals who scored high on extraversion were less likely to develop apathetic symptoms post-stroke. This finding has not been examined in a stroke population before, but it is consistent with a cross-sectional study including 286 patients with neurodegenerative diseases that showed a negative association between apathy scores and extraversion [53]. Furthermore, low conscientiousness and low openness were associated with high apathy levels at baseline in our study, which remained stable at 6-month follow-up. Also these associations have not been studied before in a stroke population, though the results were consistent with findings in a sample with mild cognitive impairment, in which retrospective change in conscientiousness from 5 years prior to assessment to baseline was positively associated with apathy, and openness was negatively associated with apathy [54].

Some controversy still exists whether depression and apathy are different, yet overlapping, disease entities. Our finding that personality traits are differentially associated with PSD and PSA suggests they are independent, at least in a stroke population [34,55]. Furthermore, our results are in agreement with the hypothesis that, besides an important role for biological factors [56], psychological factors also play a role in the development of PSD [57], and the same theory seems to be true for PSA. Hence, future studies should focus on how personality traits and other psychological factors alone and in interaction with biological factors predict the development and course of PSD and PSA. This is important for treatment and rehabilitation, as focusing on early detection of PSD and PSA might result in a better clinical outcome after stroke [58].

Strengths of this study are the longitudinal design and the low dropout rates at follow-up. In addition, validated instruments were used to evaluate the presence and level of depression, apathy, and personality traits. The consideration of the role of all five-factor personality traits in the development of both depression and apathy provides a more complete picture of the role personality traits plays in neuropsychiatric symptoms after stroke.

There are also some limitations that should be appointed. First, personality is assumed to be relatively stable over time, and studies have confirmed this partly [22], but personality traits were measured after stroke. Hence, we do not know whether and how the stroke event itself had an influence on the self-rating of personality, so the results may possibly be not completely representative for 'pre-morbid' personality, as was also reported as an unavoidable limitation in previous stroke studies on personality [30,31]. We asked the participants to fill in the questions based on their situation pre-stroke, but it might be difficult for stroke patients to retrospectively evaluate pre-stroke personality. An additional informant rating of personality could have been valuable, as the informant can indicate whether a trait was already high or low before the stroke, but also the informant rating could be influenced by the current behavior and mood state of themselves and of the stroke patient. Due to time constraints and because not every participant would have an informant we only collected self-rated personality, which has been commonly used in previous stroke studies [28,30,31].

Nevertheless, future studies should take this critical aspect into account, suggesting that they assess personality in both the stroke patient and their primary caregiver or informant. Second, different sources were used for measuring personality trait scores and psychopathology, as personality scores were based on a self-rating, while depression and apathy scores were based on a clinician-rated questionnaire. Third, no significant main effect of an interaction between personality traits and time was found. Therefore, the individual traits by time point analyses are of exploratory nature and should be treated very carefully for further interpretation. We still include them for comparison with previous studies that looked at individual time points only. Fourth, the exclusion of patients with aphasia, pre-stroke dementia, and co-morbid (neurological) conditions (e.g. Parkinson's disease, epilepsy, substance abuse) resulted in a less representative stroke sample. Lastly, patients with depressive or apathetic symptoms at an early stage might have been less motivated to participate in the study in the first place, which could have resulted in an underestimation of depression and apathy symptoms in our cohort, as the prevalence of PSA and PSD at baseline in our cohort were lower than the pooled estimated prevalences in previous meta-analyses [1,2]. In addition, the response rate for participation was relatively low (40%), which was probably due to the fact that the study was too burdensome for a large group of stroke patients. This may have resulted in a cohort with relatively mild to moderate stroke, so patients with a severe stroke might be underrepresented in our sample, as is common in these kind of studies. This again might have resulted in lower levels of PSA and PSD in our sample, although a previous study showed a similar frequency of

PSD in minor stroke [59].

5. Conclusion

Personality traits are associated with the development and sustainability of PSD or PSA. The traits associated with PSD and PSA were different, providing support for the independence of these constructs. The findings highlight the importance to take personality traits into account as a potential vulnerability factor for PSD and PSA.

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Competing interest statement

The authors have no competing interests to report.

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