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

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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

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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