Social cognition impairments are associated with behavioural changes in the long term after stroke

Britta Nijsse¹, Jacoba M. Spikman²,3, Johanna M. A. Visser-Meily⁴,5, Paul L. M. de Kort¹, Caroline M. van Heugten⁶,7,*

¹ Elisabeth-Tweesteden Hospital, Department of Neurology, Tilburg, The Netherlands, ² University of Groningen, Department of Clinical and Developmental Neuropsychology, Groningen, The Netherlands, ³ University Medical Center Groningen, Department of Neurology, Groningen, The Netherlands, ⁴ Center of Excellence in Rehabilitation Medicine, collaboration between University Medical Center Utrecht and Hoogstraat Rehabilitation, Utrecht, The Netherlands, ⁵ Brain Center Rudolf Magnus, University Medical Center Utrecht, Department of Rehabilitation, Physical Therapy Science and Sports, Utrecht, The Netherlands, ⁶ Maastricht University, Faculty of Psychology and Neuroscience, Department of Neuropsychology and Psychopharmacology, Maastricht, The Netherlands, ⁷ Maastricht University Medical Center, Faculty of Health, Medicine and Life Sciences, School for Mental Health and Neuroscience, Maastricht, The Netherlands

* c.vanheugten@maastrichtuniversity.nl

Abstract

Background and purpose

Behavioural changes after stroke might be explained by social cognition impairments. The aim of the present study was to investigate whether performances on social cognition tests (including emotion recognition, Theory of Mind (ToM), empathy and behaviour regulation) were associated with behavioural deficits (as measured by proxy ratings) in a group of patients with relatively mild stroke.

Methods

Prospective cohort study in which 119 patients underwent neuropsychological assessment with tests for social cognition (emotion recognition, ToM, empathy, and behaviour regulation) 3–4 years post stroke. Test scores were compared with scores of 50 healthy controls. Behavioural problems were assessed with the Dysexecutive Questionnaire (DEX) self rating and proxy rating scales. Pearson correlations were used to determine the relationship between the social cognition measures and DEX scores.

Results

Patients performed significantly worse on emotion recognition, ToM and behaviour regulation tests than controls. Mean DEX-self score did not differ significantly from the mean DEX-proxy score. DEX-proxy ratings correlated with tests for emotion recognition, empathy, and behavioural regulation (lower scores on these items were associated with more problems on the DEX-proxy scale).
Conclusions
Social cognition impairments are present in the long term after stroke, even in a group of mildly affected stroke patients. Most of these impairments also turned out to be associated with a broad range of behavioural problems as rated by proxies of the patients. This strengthens the proposal that social cognition impairments are part of the underlying mechanism of behavioural change. Since tests for social cognition can be administered in an early stage, this would allow for timely identification of patients at risk for behavioural problems in the long term.

Introduction
Behavioural changes are a frequent complication after stroke and may have a negative impact on the quality of life of patients, but also on the quality of life of caregivers. Since behavioural changes often relate to inadequate or inappropriate social-emotional behaviour, for example hurtful or insulting communication and emotional indifference, it is plausible to assume that social cognition impairments are part of the underlying mechanism of behavioural change. Social cognition comprises the capacities of individuals to process social information, that is, to understand the behaviour of others and to react adequately in social situations. These capacities involve different, but interrelated, processes. First, it requires the ability to recognize other people’s emotions, e.g. by facial expressions. Second, intentions, dispositions and beliefs of others have to be inferred by forming a Theory of Mind (ToM). Furthermore, one should be able to empathize with others by linking other people’s emotions to one’s own emotional experience. A final element is behaviour regulation, which involves monitoring, control and inhibition of one’s own behaviour, emotions, or thoughts, in accordance with the demands of the situation. Collectively, all these skills facilitate appropriate social behaviour. And consequently, impairments in social cognition might be related to disturbances in social-interpersonal behaviour. Social cognition impairments have been found in stroke patients, with evidence for deficits in emotion recognition, ToM and empathy. To date, the relation between these impairments and social-behavioural problems has not been investigated yet.

Since behavioural changes are commonly perceived by caregivers, they should not only be explored by patient-, but also by proxy reports. We learned from earlier research that the patients’ and relatives’ views on behavioural disturbances after stroke may differ substantially, with, in general, patients reporting less problems than relatives. This disagreement may result from patients’ impaired self-awareness, but denial may also be involved. Although denial may also play a role in relatives, their ratings of patients’ behaviour are generally considered more objective and accurate. Therefore, proxy reports are essential in assessing behavioural changes.

In patients with traumatic brain injury (TBI) proxy ratings have been used to examine the social-behavioural consequences of social cognition impairments. Spikman et al concluded that poor emotion recognition was associated with behavioural problems in TBI-patients, as rated by proxies. To our knowledge, there are no studies that investigated the behavioural consequences of social cognition impairments in stroke patients. However, according to caregivers the most frequent residual symptom identified as among the top five most important problems in stroke patients, was impaired recognition of the emotions of others (loss of...
emotional empathy), followed by ‘change in personality and behaviour’. This indicates the relevance of social cognitive and behavioural consequences of stroke.

The aim of the present study was therefore to investigate whether performances on social cognition tests (including emotion recognition, ToM, empathy and behaviour regulation) were associated with behavioural deficits in stroke patients, as measured by proxy ratings. Furthermore, self-awareness of stroke patients, and its association with social cognition deficits, was explored.

Methods
Design
The current study is an extension of the prospective longitudinal multicentre Restore4Stroke cohort study, in which stroke patients and their caregivers were followed for two years including five measurements (T1-T5). Patients were recruited from stroke units in six participating hospitals in the Netherlands between March 2011 and March 2013. For the present study patients and caregivers were asked to participate in an extra assessment at 3–4 years post stroke (T6). The T6 measurements were conducted between July 2015 and October 2016. The Restore4Stroke cohort study and the extra follow-up measurements reported here were approved by the Medical research Ethics Committees United (MEC-U).

Subjects
Patients were eligible for this study if they had a clinically confirmed diagnosis of stroke (ischemic or hemorrhagic, judged from computed tomography scan in the acute phase, according to the standard care in the participating hospitals). This is in line with the current American Stroke guidelines, which state that the diagnosis of stroke is a clinical diagnosis. Whenever the clinician was in doubt about a patient’s symptoms, magnetic resonance imaging (MRI) of the brain was performed to establish the diagnosis. All patients had to be at least 18 years old. Patients were excluded if they (1) had a serious other condition whereby an interference with the study outcomes was expected (e.g. neuromuscular disease); (2) were already dependent regarding activities of daily living (ADL) before their stroke as defined by a Barthel Index (BI) of ≤17; (3) had insufficient command of the Dutch language to understand and complete the questionnaires; or (4) were already suffering from cognitive decline as defined by a score of ≥1 on the Heteroanamnesis List Cognition before their stroke. Patients with evidence of visual neglect or a language disorder were excluded as well, because their results on the social cognition tests might have been influenced by this.

Proxies of the patients (partners, family members, friends or acquaintances) were contacted by the research assistant to fill out the Dysexecutive Questionnaire (DEX) proxy version.

Healthy controls for social cognition testing were recruited in two ways. First, partners of the participating stroke patients were asked to act as healthy controls. Second, data from an additional control group, who took part in another study, were added. These controls had been recruited from acquaintances of the researchers. Exclusion criteria were the same as for patients, with an additional exclusion criterion of the occurrence of transient ischemic attack (TIA) or stroke. Informed consent was obtained from all patients, proxies and healthy controls.

Procedure
Three-four years after stroke (T6) an extensive neuropsychological assessment was conducted by a trained research assistant (graduate neuropsychologist), either in the nearest participating
hospital or at home (if patients were not able to travel). Patients performed the total neuropsychological test battery, controls only performed the social cognition test battery.

Patients and proxies respectively filled out the DEX-self and DEX-proxy rating scale.

**Measures**

Demographic characteristics included sex, age and level of education. Patients’ level of education was recorded according to a Dutch classification system ranging from 1: did not finish primary school, to 7: university education.[19]

The hemisphere involved, the type of stroke (ischemic or hemorrhagic) and history of previous stroke(s) were obtained from medical charts. Severity of stroke was assessed with the National Institutes of Health Stroke Scale (NIHSS).[20] ADL was assessed with the BI.[21] The Bells test was used for the evaluation of visual neglect[22], and the Boston Naming Test (BNT) [23] for the evaluation of language (naming) disorder.

The Dysexecutive Questionnaire (DEX)[24] is a 20-item questionnaire, designed to measure behavioural changes that can be part of the dysexecutive syndrome. The score ranges from 0–80 (0–4 per item), with higher scores representing more severe behavioural problems. The DEX has a self rating (DEX-self) and proxy rating (DEX-proxy) version. The individual DEX items are displayed in Table 1. Since it is a broad measure, Simblett and Bateman[25], and Bodenburg and Dopslafl[26] performed factor and Rasch analyses to unravel the structure of the DEX resulting in a division into different subscales, representing different aspects of behavioural changes. Simblett and Bateman made a division into three subscales: Executive Cognition scale (DEX-EC: items 1,4, 6 and 18)[25], which measures executive functioning (planning, regulation, focussing and switching); Metacognition scale (DEX-MC: items 2, 5, 12, Table 1. Percentage of patients and proxies reporting complaints about the patient on the separate DEX-items.

| DEX-items                                      | % Patients (n = 119) | % Proxies (n = 119) |
|------------------------------------------------|---------------------|---------------------|
| 1. Problems with abstract thinking            | 73.1                | 72.3                |
| 2. Impulsivity, acting without thinking       | 70.6                | 63.9                |
| 3. Confabulation                               | 13.4                | 24.4                |
| 4. Planning problems                           | 60.5                | 58.0                |
| 5. Euphoria, excitability                      | 69.7                | 68.1                |
| 6. Temporal sequencing problems               | 61.3                | 58.8                |
| 7. Lack of insight and social awareness       | 51.3                | 47.1                |
| 8. Apathy and lack of drive                    | 72.3                | 65.5                |
| 9. Disinhibition, inappropriate behaviour      | 36.1                | 45.4                |
| 10. Variable motivation                        | 60.5                | 47.1                |
| 11. Shallow affect                             | 72.3                | 61.3                |
| 12. Losing temper, aggression                  | 73.9                | 76.5                |
| 13. Lack of concern                            | 45.4                | 49.6                |
| 14. Perseveration                              | 55.5                | 51.3                |
| 15. Restlessness                               | 66.4                | 53.8                |
| 16. Inability to inhibit responses             | 59.7                | 58.0                |
| 17. Knowing-doing dissociation                 | 53.8                | 45.4                |
| 18. Distractibility                            | 80.7                | 73.1                |
| 19. Loss of decision making ability            | 73.9                | 63.9                |
| 20. Unconcern for social rules                 | 68.9                | 64.7                |

DEX = Dysexecutive Questionnaire.

https://doi.org/10.1371/journal.pone.0213725.t001
which measures awareness and understanding of one’s own thought processes; and Behavioural-Emotional Selfregulation scale (DEX-BESR: items 3, 7, 8, 10, 13, 14, 15 and 17)\[25\], which measures functions that are involved in emotional and reward processing, necessary for appropriate adaptive responding to others. Bateman and Dopslaff defined a fourth subscale: the Social Convention scale (DEX-SC: items 9, 12, 13 and 20)\[26\], which measures awareness of social conventions and the ability to incorporate social interaction in one’s own behaviour. The DEX-BESR and DEX-SC subscales represent measures of social-emotional processes in behaviour, while DEX-EC and DEX-MC scales are more rational scales, measuring executive functioning and reflection on one’s own behaviour respectively. The four subscales were used in our analyses.

To measure social cognition, tests were chosen that were designed to measure emotion recognition, ToM, empathy, and behaviour regulation.

**Emotion recognition.** The Ekman 60-Faces test of the Facial Expression of Emotion: Stimuli and Tests (FEEST)\[27\] was used to examine the recognition of emotional expressions on faces. Sixty faces were shown, with expressions depicting the primary emotions Fear, Disgust, Anger, Happiness, Sadness, or Surprise (maximum score per emotion = 10). Stimuli were presented for 3 seconds. The total score ranges from 0–60, with higher scores indicating better emotion recognition.

**Theory of mind.** The Cartoon test\[7\] is a test for ToM. Subjects had to describe 12 cartoons displaying humorous situations. In half of them, the joke is based on the false belief or ignorance of a character in the cartoon, and the subject needs to form a ToM in order to understand the joke. The other cartoons only require mental state attribution of the person who drew the cartoon in order to understand his humorous intention. The score ranges from 0–36 (0–3 per item), with a higher score denoting better performance. With a short version of the Faux Pas test\[28\] the capacity to judge the inappropriateness of behaviour in social situations was assessed. A faux pas occurs when someone says something awkward, hurtful, or insulting to another person, not realizing that one should not say it. Recognizing a faux pas requires belief attribution and inferences about a person’s feelings. The task consists of 10 short stories, half of which describing a situation comprising a social faux pas. The Faux Pas Detection score ranges from 0–10 (higher score indicating better detection).

**Empathy.** In the five faux pas items of the Faux Pas test participants are asked to describe the feelings of the faux pas victim. These responses form the Faux Pas Empathy score, ranging from 0–5, with a higher score indicating greater empathic ability. Various aspects of emotional empathy were assessed using the Dutch version of the Balanced Emotional Empathy Scale (BEES) \[29\]. This is a 30-item questionnaire, on which subjects rate the extent to which they agree with each statement (ranging from −4 to 4), for example: "Unhappy movie endings haunt me for hours" or "I cannot feel much sorrow for those who are responsible for their own misery" (total score ranging from -120 to 120). Higher scores represent higher levels of emotional empathy.

**Behaviour regulation and inhibition.** The Hayling Sentence Completion test\[30\] consists of two sets of 15 sentences each having the last word missing. In the first section the examiner reads each sentence aloud and the participant has to simply complete the sentences, yielding a simple measure of response initiation speed. The second part requires subjects to complete a sentence with a nonsense ending word (and suppress a sensible one), giving measures of response suppression ability and thinking time. Total scaled score ranges from 1 (impaired) to 10 (very superior).
Statistical analyses

Descriptive statistics were used to describe patients’ characteristics. Chi-square and t-tests were used to compare demographic characteristics between patients and controls. Each DEX-item was dichotomized, with a complaint being absent or present. Descriptive statistics were used to calculate frequencies of the complaints of patients and proxies.

Preliminary analyses were conducted to ensure no violation of the assumption of normality on all social cognition tests and DEX-scores.

Analysis of covariance (ANCOVA) was used to explore differences between patients and controls on all social cognition tests, in which the selection of covariates was based on demographic differences between groups. Effect sizes (Cohen’s d) were calculated using means and standard deviations. T-tests were used to compare test results between vertebrobasilar and anterior circulation patients, and to compare left- versus right-hemisphere patients.

T-tests were used to compare mean DEX-self scores and DEX-proxy scores. DEX difference scores were calculated (DEX-dif = DEX-self minus DEX-proxy) as an indication of self-awareness. Pearson correlations were used to determine the relationship between the social cognition measures and the DEX-self, DEX-proxy and DEX-dif scores, and the four DEX subscales (calculated from the DEX-proxy score).

The critical value of alpha was set at 0.05. Analyses were performed with IBM SPSS Statistics version 19.

Results

A total of 395 patients were included in the Restore4Stroke cohort study. At T6, 160 of them (40.5%) were eligible for further testing. With respect to the 235 resigned patients, 33 patients died, 120 patients refused further participation, 47 patients could not be reached by T6, and in 35 patients it was not possible to conduct the T6 assessment because of their general physical condition. Two patients had evidence of visual neglect according to the results of the Bells test, ten patients had evidence of language disorder according to the results of the BNT or the clinical judgement of the neuropsychologist. They were all excluded, which resulted in a total of 148 patients. In 119 patients, both DEX self reports and DEX proxy reports were available, so they were included in the present study.

The demographic and stroke-related characteristics of these 119 patients are displayed in Table 2. At T6 mean age was 67.9 years (SD10.8), and mean time since stroke was 3.7 years (SD0.7).

Fifty controls (half of which were partners) with a mean age of 65.2 years (SD8.1) were included. Chi-square and t-tests showed no significant differences between patients and controls with respect to age (t = -1.8, p = 0.077) and education level (high-education: controls 40.0% vs patients 27.7%, X^2 = 2.5, p = 0.117), while there were more men in the patient group (patients 70.6% vs controls 48.0%, X^2 = 7.8, p = 0.005). Therefore, sex was included as covariate in the ANCOVA.

In Table 3 the means and SDs on the social cognition tests are presented for both the patients and the control group. Patients performed significantly worse on the FEEST total score and FEEST emotion Anger (emotion recognition), Cartoon test (ToM), and Hayling (behaviour regulation).

Table 4 shows the mean scores in the different subgroups (vertebrobasilar versus anterior circulation, and left- versus right-hemisphere). No significant differences were found between subgroups.

Mean DEX-self score was 20.1 (SD11.5), and mean DEX-proxy score was 19.3 (SD13.4); t = 0.672, p = 0.503. On the DEX subscale items there was a significant difference between the
DEX-EC self score and proxy score (mean self score = 5.0 (SD 3.4) vs mean proxy score = 4.3 (SD 3.2); \( t = 2.1, p = 0.042 \)). On the other 3 subscales there were no significant differences.

In Table 1 the separate DEX-items are listed along with the frequencies of the complaints of patients and proxies. The behavioural problems most frequently mentioned by patients were 1) distractibility, 2) loss of decision making ability, and 3) aggression. The behavioural problems most frequently mentioned by proxies were 1) aggression, 2) distractibility, and 3) problems with abstract thinking. On most items there were more patients than proxies reporting problems.

Correlations between social cognition test results in patients and the DEX-self, DEX-proxy, and DEX-dif scores are shown in Table 5. Concerning the DEX-proxy ratings, significant but weak correlations were found with the FEEST total score, FEEST Anger score, FEEST Disgust score, the Hayling score, and the BEES score (lower scores on these items were associated with more problems on the DEX-proxy scale). Thus, the worse the emotion recognition performance and the lower the scores on behaviour regulation and empathy in patients, the more behavioural problems were indicated by the proxy. The FEEST Anger score, the Faux-Pas empathy score, and the Hayling score correlated significantly with the DEX-dif score (lower scores on the FEEST Anger score, Faux-Pas empathy score, and Hayling score were associated with a lower DEX-dif score).

Table 6 shows the correlations between the social cognition test results and the four DEX subscale scores that were calculated from the DEX-proxy score. All significant correlation

| Table 2. Characteristics of stroke patients (n = 119) and controls (n = 50). |
|-----------------------------|-----------------------------|-----------------------------|
|                             | patients, n (%)             | controls, n (%)              |
| Sex, number of men          | 84 (70.6%)                  | 24 (48.0%)                  |
| Age in years; mean (SD)     |                             |                             |
| T1                          | 64.3 (±11.0)                | 65.2 (±8.1)                 |
| T6                          | 67.9 (±10.8)                |                             |
| Education level             |                             |                             |
| Low (1–5)                   | 86 (72.3%)                  | 30 (60.0%)                  |
| High (6–7)                  | 33 (27.7%)                  | 20 (40.0%)                  |
| Stroke characteristics      |                             |                             |
| Type of stroke              |                             |                             |
| Ischemic                    | 111 (93.3%)                 |                             |
| Haemorrhagic                | 8 (6.7%)                    |                             |
| Location of stroke          |                             |                             |
| Left anterior circulation   | 38 (31.9%)                  |                             |
| Right anterior circulation  | 50 (42.0%)                  |                             |
| Vertebrobasilar             | 31 (26.1%)                  |                             |
| Recurrent stroke            | 17 (14.3%)                  |                             |
| NIHSS score at T1; median (SD)| 2.0 (±3.1)                      |                             |
| No stroke symptoms (NIHSS 0)| 31 (26.1%)                  |                             |
| Minor stroke symptoms (NIHSS 1–4)| 65 (54.6%)                    |                             |
| Moderate stroke symptoms (NIHSS 5–12)| 21 (17.6%)                   |                             |
| Moderate to severe symptoms (NIHSS>12)| 2 (1.7%)                    |                             |
| Barthel Index at T1         |                             |                             |
| ADL independent (BI 19–20)  | 68 (57.1%)                  |                             |
| ADL dependent (BI <19)      | 51 (42.9%)                  |                             |

T1 = 4 days after stroke; NIHSS = National Institutes of Health Stroke Scale.

https://doi.org/10.1371/journal.pone.0213725.t002

DEX-EC self score and proxy score (mean self score = 5.0 (SD 3.4) vs mean proxy score = 4.3 (SD 3.2); \( t = 2.1, p = 0.042 \)). On the other 3 subscales there were no significant differences.

In Table 1 the separate DEX-items are listed along with the frequencies of the complaints of patients and proxies. The behavioural problems most frequently mentioned by patients were 1) distractibility, 2) loss of decision making ability, and 3) aggression. The behavioural problems most frequently mentioned by proxies were 1) aggression, 2) distractibility, and 3) problems with abstract thinking. On most items there were more patients than proxies reporting problems.

Correlations between social cognition test results in patients and the DEX-self, DEX-proxy, and DEX-dif scores are shown in Table 5. Concerning the DEX-proxy ratings, significant but weak correlations were found with the FEEST total score, FEEST Anger score, FEEST Disgust score, the Hayling score, and the BEES score (lower scores on these items were associated with more problems on the DEX-proxy scale). Thus, the worse the emotion recognition performance and the lower the scores on behaviour regulation and empathy in patients, the more behavioural problems were indicated by the proxy. The FEEST Anger score, the Faux-Pas empathy score, and the Hayling score correlated significantly with the DEX-dif score (lower scores on the FEEST Anger score, Faux-Pas empathy score, and Hayling score were associated with a lower DEX-dif score).

Table 6 shows the correlations between the social cognition test results and the four DEX subscale scores that were calculated from the DEX-proxy score. All significant correlation
coefficients were negative, indicating that worse performances on the social cognition test measures were associated with more problems on the DEX subscales reported by the proxy.

Discussion

Our study found a significant relationship between deficits in emotion recognition, empathy and behaviour regulation in stroke patients, and behavioural changes reported by significant others. This finding supports the hypothesis that deficits in aspects of social cognition may underlie behavioural deficits after stroke.

Stroke patients performed significantly worse than healthy controls on social cognition tests measuring emotion recognition, ToM and behaviour regulation in the long term after stroke. This is in line with previous studies.[6–10] It is interesting to find that social cognition impairments and behavioural changes after stroke

Table 3. Social cognition test results 3–4 years after stroke.

| Test measures          | Stroke patients (n = 119) Mean (SD) | Healthy controls (n = 50) Mean (SD) | ANCOVA            |
|------------------------|-------------------------------------|-------------------------------------|-------------------|
|                        |                                     |                                     | F  | p-value | Effect size |
| FEEST total score      | 42.66 (6.2)                         | 45.02 (6.2)                         | 4.26 | 0.041   | 0.38        |
| FEEST-anger            | 6.69 (2.2)                          | 7.79 (1.9)                          | 7.98 | 0.005   | 0.54        |
| FEEST-disgust          | 6.69 (2.4)                          | 7.27 (2.1)                          | 0.90 | 0.346   | 0.26        |
| FEEST-fear             | 4.70 (2.2)                          | 4.81 (2.5)                          | 0.55 | 0.460   | 0.05        |
| FEEST-happiness        | 9.73 (0.6)                          | 9.79 (0.5)                          | 0.071 | 0.790 | 0.11        |
| FEEST-sadness          | 6.06 (2.0)                          | 6.50 (1.8)                          | 1.58 | 0.210   | 0.23        |
| FEEST-surprise         | 8.78 (1.5)                          | 8.85 (1.2)                          | 0.069 | 0.793 | 0.05        |
| Cartoon test           | 21.04 (6.9)                         | 22.75 (5.9)                         | 5.59 | 0.019   | 0.27        |
| Faux Pas detection     | 9.21 (1.0)                          | 9.12 (0.7)                          | 0.34 | 0.563   | -0.10       |
| Faux Pas empathy       | 2.99 (1.2)                          | 3.28 (1.2)                          | 1.05 | 0.306   | 0.24        |
| Hayling                | 3.02 (1.8)                          | 4.65 (1.4)                          | 32.32 | <0.001 | 1.01        |
| BEES                   | 32.22 (21.5)                        | 35.60 (26.1)                        | 0.035 | 0.852   | 0.14        |

FEEST = Facial Expression of Emotion: Stimuli and Tests; BEES = Balanced Emotional Empathy Scale.

https://doi.org/10.1371/journal.pone.0213725.t003

Table 4. Comparisons of mean scores between subgroups.

|                        | Anterior circulation (n = 86) | Vertebrobasilar circulation (n = 30) | p-value |
|------------------------|------------------------------|--------------------------------------|---------|
| FEEST                  | 42.7                         | 42.5                                 | 0.893   |
| Cartoons               | 20.9                         | 21.4                                 | 0.762   |
| Faux Pas detection     | 9.2                          | 9.3                                  | 0.464   |
| Faux Pas empathy       | 3.0                          | 2.9                                  | 0.494   |
| Hayling                | 3.0                          | 3.1                                  | 0.686   |
| BEES                   | 32.9                         | 30.3                                 | 0.573   |
| Left hemisphere (n = 36)|                              | Right hemisphere (n = 50)            |         |
| FEEST                  | 42.3                         | 43.0                                 | 0.639   |
| Cartoons               | 21.4                         | 20.6                                 | 0.612   |
| Faux Pas detection     | 9.1                          | 9.2                                  | 0.732   |
| Faux Pas empathy       | 2.9                          | 3.1                                  | 0.399   |
| Hayling                | 2.9                          | 3.0                                  | 0.890   |
| BEES                   | 36.2                         | 30.6                                 | 0.263   |

FEEST = Facial Expression of Emotion: Stimuli and Tests; BEES = Balanced Emotional Empathy Scale.

https://doi.org/10.1371/journal.pone.0213725.t004
impairments are still present at such a long time after stroke, even in a group of mildly affected stroke patients. The majority of our patients (80.7%) suffered a minor stroke (NIHSS $<5$). Still, social cognition impairments were found in this relatively non-disabled patient population. It could, however, explain why we did not find differences between right- and left hemisphere stroke patients. Deficits in social cognition are associated with lesions in the right prefrontal cortex, the right superior temporal gyrus, and the temporo-parietal junction.[31] Generally, minor strokes do not affect these areas, as most of them are lacunar infarcts involving small penetrating arteries in the deep areas of the brain. In many studies comparing social cognition in right-and left hemisphere strokes, lacunar infarcts were excluded or comprised just a small amount of all strokes.[6] We also did not find differences between vertebrobasilar and anterior circulation stroke patients. One would expect that social cognition impairments are less common in vertebrobasilar circulation patients, but impairments are known to be present in this group as well. In recent literature, the association between vertebrobasilar stroke or other cerebellar diseases, and impaired emotion recognition was found.[32–34] Furthermore, functional MRI studies showed that the cerebellum is critically implicated in social cognition.[35,36]

It is up for discussion whether age and educational level should also have been included as covariates in the ANCOVA, because chi-square and t-tests on differences between patients and controls approached significance on these factors (age: $t = -1.8$, $p = 0.08$; and education level: $X^2 = 2.5$, $p = 0.12$). Therefore, we also performed these analyses, and found that the results on the FEEST and Cartoon test did no longer differ between patients and controls (S1 Table). However, we feared that applying these ANCOVA’s may imply a form of overcorrection, which might even lead to a type II error. We deem it of clinical relevance to signal even mild impairments in social cognition in this group; not detecting effects that are there (type II error), prohibiting patients from getting the appropriate care, would in our opinion be more harmful for patients than the reverse (type I error). Hence, we presented the ANCOVA with sex as the only covariate, since this was the only demographic factor which differed significantly between patients and controls.

### Table 5. Correlations between social cognition test results in patients and DEX-scores.

|                          | DEX-self | DEX-proxy | DEX-dif (self − proxy) |
|--------------------------|----------|-----------|------------------------|
| FEEST total score        | -0.217** | -0.254**  | 0.072                  |
| FEEST-anger              | -0.021   | -0.225**  | 0.216**                |
| FEEST-disgust            | -0.268*  | -0.277*   | 0.050                  |
| FEEST-fear               | -0.155   | -0.050    | -0.086                 |
| FEEST-happiness          | -0.067   | -0.069    | 0.012                  |
| FEEST-sadness            | -0.197** | -0.115    | -0.056                 |
| FEEST-surprise           | 0.091    | -0.016    | 0.098                  |
| Cartoons                 | -0.071   | -0.137    | 0.079                  |
| Faux-Pas detection       | -0.121   | 0.082     | -0.192**               |
| Faux-Pas empathy         | 0.092    | -0.166    | 0.249*                 |
| Hayling                  | -0.087   | -0.265*   | 0.195**                |
| BEES                     | -0.091   | -0.195**  | 0.121                  |

FEEST = Facial Expression of Emotion: Stimuli and Tests; BEES = Balanced Emotional Empathy Scale; DEX = Dysexecutive Questionnaire

* $p<0.01$

** $p<0.05$

https://doi.org/10.1371/journal.pone.0213725.t005
Mean DEX-scores were higher on the DEX-self rating version than on the DEX-proxy rating version, indicating that patients reported more problems about themselves than proxies did about them. As a consequence mean DEX-dif score was positive, which could be interpreted as normal self-awareness. However, lower DEX-dif scores correlated significantly with lower scores on the FEEST Anger, Faux-Pas empathy and Hayling. Hence, impaired self-awareness is likely to be related to deficits in social cognition, such as emotion recognition (anger), empathy and behaviour regulation. Although mean DEX-dif score was positive, 38.7% of patients had a negative DEX-dif score (i.e., these patients reported less problems than proxies did about them).

In the study of Spikman et al[14], mean DEX-self and DEX-proxy scores in their patient group with moderate to severe TBI were higher than in our present group of stroke patients. In TBI-patients (especially severe TBI), prefrontal brain damage is commonly found since prefrontal areas are specifically vulnerable to TBI. It is known that the presence of social behavioural problems is related to damage to inferior and medial prefrontal areas.[37,38] Generally, (minor) strokes do not affect these prefrontal areas. This might explain why TBI patients and their proxies may experience more behavioural problems, and thus, why mean DEX scores in TBI patients are higher than in our stroke patients. Nevertheless, even in stroke patients with a relatively favorable outcome (in terms of stroke severity), behavioural problems were found. This suggests that we should look beyond the location of brain injury by studying cerebral networks.[39] It is well known that stroke not only affects local connectivity but can also cause remote brain changes, as shown by functional MRI, Positron Emission Tomography (PET), and diffusion tensor imaging (DTI) studies.[40] Voxel-based lesion-symptom mapping results in patients with penetrating TBI showed that impairment in facial emotion recognition was due to damage in a bilateral fronto-temporo-limbic network, including medial prefrontal cortex, anterior cingulate cortex, left insula and temporal areas.[41] In patients who underwent resection of a low-grade glioma, lesion-symptom mapping showed that impairments in ToM were mainly related to the disruption of right fronto-parietal connectivity, and more specifically, to the degree of disconnection in the arcuate fasciculus and the cingulum.[42,43] Although lesion-symptom mapping studies on social cognition in stroke patients are lacking, it might be possible that even a minor stroke may interrupt a cerebral network, which is involved in social cognition processing.[39,44] Whether DTI-based measures of brain connectivity predict social cognition impairments as well is currently being investigated by the Prediction of Cognitive Recovery After Stroke (PROCRAS) investigators.[45]

The DEX is a broad measure of behavioural problems collectively known as the dysexecutive syndrome, that is, changes in emotion, personality, motivation, behaviour, executive...
functioning and cognition. The four subscales were designed to measure these different aspects separately. In relation to social cognition, we were most interested in the DEX-SC and DEX-BESR subscales, which measure social-emotional processes in behaviour. In addition to our overall finding that deficits on social cognition tasks were significantly, though weakly, related to behavioural problems in daily life, we found specific relationships between separate aspects of social cognition and separate categories of behavioural problems, represented by the different DEX subscales. Emotion recognition was related to all four subscales, but the Faux-Pas empathy (which is a reflection on feelings of a character in the Faux-Pas stories) only related to the two social-emotional subscales. The BEES, another indication of empathy, but measuring someone’s empathic reaction in hypothetical situations, was related to both the DEX-SC, the DEX-MC, and the DEX-EC subscales, but not to the DEX-BESR subscale. The Hayling, measuring behavioural regulation and inhibition, was in addition to the social-emotional subscales also related to the DEX-EC subscale, reflecting that the ability to stop behaviour is also important in executive task conditions. Correlations between the social cognition measures and the DEX subscales were not substantially different from the correlations with the total proxy score.

Just like emotional and cognitive problems, social cognitive and behavioural problems are invisible consequences of stroke. The invisibility of these consequences and the fact that stroke patients may experience impaired self-awareness, may lead to difficult situations in relationships and family. Relatives may feel at their wit’s end as they don’t understand the patients’ behaviour and eventually can’t handle the situation anymore. Now we know that there is a correlation between social cognition impairments and behavioural problems, the next step would be the identification of patients at risk of behavioural problems, so that targeted therapy can be given. Although only cross-sectional data were presented, and no statement can be made about causality, it is conceptually quite obvious that impairments in social information processing are underlying social behaviour, and not vice versa. Since social cognition tests can be performed in the acute stages after stroke, whereas behavioural problems only reveal themselves in the course of time, early detection of social cognition problems might contribute to the identification of patients at risk of behavioural problems. In this group of patients, focused psycho-education can be given to both patients and relatives. Also, when social cognition impairments are present, specific social cognitive treatment can be started, which has been proven effective in TBI patients.[46] Although this treatment may also be effective in stroke patients, this is a topic for further investigation.

One of the strengths of our study is that the most salient aspects of social cognition were assessed in a large sample of stroke patients. Moreover, we are the first to study the relationship between social cognition and behavioural changes after stroke, based on proxy ratings.

Some limitations of our study should be mentioned. First, no brain-imaging characteristics were assessed in our study. This could have told us more about lesion sites. Second, a disadvantage of examining social cognition in the long term after stroke is that only the most motivated patients may be willing to participate in extensive neuropsychological assessment. Nevertheless, no significant differences were found in stroke characteristics between the 119 patients left at T6 and the resigned patients. Another limitation is that we could not guarantee that all participating patients were free of pre-history personality problems that might have influenced performances on social cognition tests, or might have played a role in behavioural problems. Presence of psychiatric problems was not an exclusion criterion. Furthermore, the use of partners as healthy controls is a matter of debate, as they may not be naive to the purpose of the study, and their own behaviour may reflect or over-compensate social deficits in the patient they live with. Finally, since our study contains cross-sectional data, we could only examine the relationship between social cognition and behaviour in the long term. More research is
needed to assess whether social cognition impairments in the acute stages after stroke can predict behavioural problems in the long term.

Conclusions

Social cognition impairments are present in the long term after stroke, even in a group of mildly affected stroke patients. Most of these impairments also turned out to be associated with a broad range of behavioural problems as rated by proxies of the patients. Although only cross-sectional data were presented, this strengthens the proposal that social cognition impairments are part of the underlying mechanism of behavioural change. When patients at risk of behavioural problems could be identified in the early stages after stroke by performing social cognition tests, targeted social cognitive treatment can be given. Whether such treatment, that has been proven effective in TBI patients, is also effective in stroke patients, is a topic for further investigation.

Supporting information

S1 Table. Social cognition test results 3–4 years after stroke (ANCOVA with sex, age and educational level as covariates).

(SAV)

S1 Dataset. SPSS data file.

Author Contributions

Conceptualization: Jacoba M. Spikman, Johanna M. A. Visser-Meily, Paul L. M. de Kort, Caroline M. van Heugten.

Data curation: Britta Nijsse, Jacoba M. Spikman.

Formal analysis: Britta Nijsse, Jacoba M. Spikman.

Funding acquisition: Britta Nijsse, Jacoba M. Spikman, Johanna M. A. Visser-Meily, Paul L. M. de Kort, Caroline M. van Heugten.

Investigation: Britta Nijsse.

Methodology: Jacoba M. Spikman, Johanna M. A. Visser-Meily, Paul L. M. de Kort, Caroline M. van Heugten.

Project administration: Britta Nijsse.

Resources: Britta Nijsse.

Software: Britta Nijsse.

Supervision: Jacoba M. Spikman, Johanna M. A. Visser-Meily, Paul L. M. de Kort, Caroline M. van Heugten.

Writing – original draft: Britta Nijsse.

Writing – review & editing: Jacoba M. Spikman, Johanna M. A. Visser-Meily, Paul L. M. de Kort, Caroline M. van Heugten.
References

1. Ferro JM, Caeiro L, Santos C. Poststroke emotional and behavior impairment: a narrative review. Cerebrovasc Dis 2009; 27 Suppl 1:197–203.

2. Henry JD, Von Hippel W, Molenberghs P, Lee T, Sachdev PS. Clinical assessment of social cognitive function in neurological disorders. Nature Reviews Neurology 2016; 12(1):28–39. https://doi.org/10.1038/nrneurol.2015.229 PMID: 26670297

3. Adolphs R. Social cognition and the human brain. Trends Cogn Sci (Regul Ed) 1999; 3(12):469–479.

4. Frith CD, Frith U. Social cognition in humans. Current Biology 2007; 17(16):R724–R732. https://doi.org/10.1016/j.cub.2007.05.068 PMID: 17714666

5. Bandura A. Social cognitive theory of self-regulation. Organ Behav Hum Decis Process 1991; 50(2):248–287.

6. Yuvaraj R, Murugappan M, Norlinah MI, Sundaraj K, Khairiyah M. Review of emotion recognition in stroke patients. Dement Geriatr Cogn Disord 2013; 36(3–4):179–196. https://doi.org/10.1159/000353440 PMID: 23899462

7. Happé F, Brownell H, Winner E. Acquired theory of mind impairments following stroke. Cognition 1999; 70(3):211–240. PMID: 10384736

8. Martín-Rodríguez JF, León-Carrion J. Theory of mind deficits in patients with acquired brain injury: A quantitative review. Neuropsychologia 2010; 48(5):1181–1191. https://doi.org/10.1016/j.neuropsychologia.2010.02.009 PMID: 20153762

9. Yeh Z, Tsai C. Impairment on theory of mind and empathy in patients with stroke. Psychiatry Clin Neurosci 2014; 68(8):612–620. https://doi.org/10.1111/pcn.12173 PMID: 24521285

10. Hillis AE. Inability to empathize: brain lesions that disrupt sharing and understanding another’s emotions. Brain 2014 Apr; 137(Pt 4):981–997. https://doi.org/10.1093/brain/awt317 PMID: 24293265

11. Hochstenbach J, Prigatano G, Mulder T. Patients’ and relatives’ reports of disturbances 9 months after stroke: subjective changes in physical functioning, cognition, emotion, and behavior. Arch Phys Med Rehabil 2005; 86(8):1587–1593. https://doi.org/10.1016/j.apmr.2004.11.050 PMID: 16084812

12. Milders M, Fuchs S, Crawford JR. Neuropsychological impairments and changes in emotional and social behaviour following severe traumatic brain injury. Journal of clinical and experimental neuropsychology 2003; 25(2):157–172. https://doi.org/10.1076/jcen.25.2.157.13642 PMID: 12754675

13. Milders M, Ietswaart M, Crawford JR, Currie D. Social behavior following traumatic brain injury and its association with emotion recognition, understanding of intentions, and cognitive flexibility. Journal of the International Neuropsychological Society 2008; 14(2):318–326. https://doi.org/10.1017/S1355617708080351 PMID: 18282329

14. Spikman JM, Milders MV, Visser-Keizer AC, Westerhof-Evers HJ, Herben-Dekker M, van der Naalt J. Deficits in facial emotion recognition indicate behavioral changes and impaired self-awareness after moderate to severe traumatic brain injury. PloS one 2013; 8(6):e65581. https://doi.org/10.1371/journal.pone.0065581 PMID: 23776505

15. Hillis AE, Tippett DC. Stroke recovery: Surprising influences and residual consequences. Advances in medicine 2014; 2014.

16. Mierlo ML, Heugten CM, Post MW, Lindeman E, Kort PL, Visser-Meily J. A longitudinal cohort study on quality of life in stroke patients and their partners: Restore4Stroke Cohort. International Journal of Stroke 2014; 9(1):148–154. https://doi.org/10.1111/ijis.12055 PMID: 22974050

17. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2018 Mar; 49(3):e46–e110. https://doi.org/10.1161/STR.118.1000000000158 PMID: 29367334

18. Meijer R, van Limbeek J, de Haan R. Development of the Stroke-unit Discharge Guideline: choice of assessment instruments for prediction in the subacute phase post-stroke. Int J Rehabil Res 2006 Mar; 29(1):1–8. https://doi.org/10.1097/01.mrr.0000175289.59788.41 PMID: 16432383

19. Verhage F. Intelligentie en leeftijd: Onderzoek bij Nederlanders van twaalf tot zevenenzeventig jaar.: Van Gorcum Assen; 1964.

20. Brott T, Adams HP Jr, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurements of acute cerebral infarction: a clinical examination scale. Stroke 1989 Jul; 20(7):864–870. PMID: 2749846

21. Collin C, Wade D, Davies S, Home V. The Barthel ADL index: a reliability study. Disability & Rehabilitation 1988; 10(2):61–63.

22. Gauthier L, Dehaut F, Joanette Y. The bells test: a quantitative and qualitative test for visual neglect. International journal of clinical neuropsychology 1989; 11(2):49–54.

23. Kaplan E. The assessment of aphasia and related disorders. Lippincott Williams & Wilkins; 1983.
24. Wilson BA, Evans JJ, Alderman N, Burgess PW, Emslie H. Behavioural assessment of the dysexecutive syndrome. Methodology of frontal and executive function 1997:239–250.
25. Simblett SK, Bateman A. Dimensions of the Dysexecutive Questionnaire (DEX) examined using Rasch analysis. Neuropsychological rehabilitation 2011; 21(1):1–25. https://doi.org/10.1080/09602011.2010.531216 PMID: 21181602
26. Bodenburg S, Dopsiaff N. The Dysexecutive Questionnaire advanced: item and test score characteristics, 4-factor solution, and severity classification. J Nerv Ment Dis 2008 Jan; 196(1):75–78. https://doi.org/10.1097/NMD.0b013e3181f5aa2b PMID: 18195646
27. Young A, Perrett D, Calder A, Sprengelmeyer R, Ekman P. Facial expressions of emotion: Stimuli and tests (FEEST). 2002. Bury St. Edmunds, UK, Thames Valley Test Company. Ref Type: Computer Program.
28. Stone VE, Baron-Cohen S, Knight RT. Frontal lobe contributions to theory of mind. J Cogn Neurosci 1998; 10(5):640–656. PMID: 9802997
29. Mehrabian A. Beyond IQ: Broad-based measurement of individual success potential or “emotional intelligence”. Genet Soc Gen Psychol Monogr 2000; 126(2):133. PMID: 10846622
30. Burgess PW, Shallice T. The hayling and brixton tests. 1997; Thames Valley Test Company, Bury St. Edmunds, U.K.
31. Van Overwalle F. Social cognition and the brain: a meta-analysis. Hum Brain Mapp 2009; 30(3):829–858. https://doi.org/10.1002/hbm.20547 PMID: 18381770
32. Wilkos E, Brown TJ, Slawinska K, Kucharska KA. Social cognitive and neurocognitive deficits in inpatients with unilateral thalamic lesions—study. Neuropsychiatr Dis Treat 2015 Apr 10; 11:1031–1038. https://doi.org/10.2147/NDT.S78037 PMID: 25914535
33. Harciarek M, Heilman KM. The contribution of anterior and posterior regions of the right hemisphere to the recognition of emotional faces. Journal of clinical and experimental neuropsychology 2009; 31 (3):322–330. https://doi.org/10.1080/13803390802119930 PMID: 18608696
34. Hoche F, Guell X, Sherman JC, Vangel MG, Schmahmann JD. Cerebellar contribution to social cognition. The Cerebellum 2016; 15(6):732–743. https://doi.org/10.1007/s12311-015-0746-9 PMID: 26585120
35. Van Overwalle F, Baetens K, Marin P, Vandekerckhove M. Social cognition and the cerebellum: a meta-analysis of over 350 fMRI studies. Neuroimage 2014; 96:554–572. https://doi.org/10.1016/j.neuroimage.2013.09.033 PMID: 24076206
36. Zinchenko O, Yaple ZA, Arsalidou M. Brain responses to dynamic facial expressions: a normative meta-analysis. Frontiers in Human Neuroscience 2018; 12.
37. Zappala G, de Schotten MT, Eslinger PJ. Traumatic brain injury and the frontal lobes: what can we gain with diffusion tensor imaging? Cortex 2012; 48(2):156–165. https://doi.org/10.1016/j.cortex.2011.06.020 PMID: 21813118
38. Stuss DT. Traumatic brain injury: relation to executive dysfunction and the frontal lobes. Curr Opin Neurol 2011 Dec; 24(6):584–589. https://doi.org/10.1097/WCO.0b013e3283d7eb8 PMID: 21968550
39. Kennedy DP, Adolphs R. The social brain in psychiatric and neurological disorders. Trends Cogn Sci (Regul Ed) 2012; 16(11):559–572.
40. Lim JS, Kang DW. Stroke Connectome and Its Implications for Cognitive and Behavioral Sequela of Stroke. J Stroke 2015 Sep; 17(3):256–267. https://doi.org/10.5853/jos.2015.17.3.256 PMID: 26437992
41. Dal Monte O, Krueger F, Solomon JM, Schintu S, Knutson KM, Strenziok M, et al. A voxel-based lesion study on facial emotion recognition after penetrating brain injury. Social cognitive and affective neuroscience 2012; 8(6):632–639. https://doi.org/10.1093/scan/nss041 PMID: 22496440
42. Herbet G, Lafargue G, Bonnetblanc F, Mortez-Gasser S, Menjot de Champfleur N, Duffau H. Inferring a dual-stream model of mentalizing from associative white matter fibres disconnection. Brain 2014; 137 (3):944–959.
43. Nakajima R, Yordanova YN, Duffau H, Herbet G. Neuropsychological evidence for the crucial role of the right arcuate fasciculus in the face-based mentalizing network: A disconnection analysis. Neuropsychologia 2018; 115:179–187. https://doi.org/10.1016/j.neuropsychologia.2018.01.024 PMID: 29360518
44. Limongi R, Tomio A, Ibanez A. Dynamical predictions of insular hubs for social cognition and their application to stroke. Front Behav Neurosci 2014 Nov 4; 8:380. https://doi.org/10.3389/fnbeh.2014.00380 PMID: 25408640
45. Aben HP, Reijmer YD, Visser-Meily JM, Spikman JM, de Bresser J, Bisselers GJ, et al. A Role for New Brain Magnetic Resonance Imaging Modalities in Daily Clinical Practice: Protocol of the Prediction of Cognitive Recovery After Stroke (PROCRAST) Study. JMIR Res Protoc 2018 May 28; 7(5):e127. https://doi.org/10.2196/resprot.9431 PMID: 29807883
46. Westerhof-Evers HJ, Visser-Keizer AC, Fasotti L, Schonherr MC, Vink M, van der Naalt J, et al. Effectiveness of a Treatment for Impairments in Social Cognition and Emotion Regulation (T-ScEmo) After Traumatic Brain Injury: A Randomized Controlled Trial. J Head Trauma Rehabil 2017 Sep/Oct; 32 (5):296–307. https://doi.org/10.1097/HTR.0000000000000332 PMID: 28786854