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Principles of proportional recovery after stroke generalize to neglect and aphasia

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ABSTRACT

Background: Motor recovery after stroke can be characterized by two strictly different patterns. A majority of patients recover about 70% of initial impairment, while some patients with severe initial deficits show little or no improvement. Here, we investigated whether recovery from visuospatial neglect and aphasia is also separated into two different groups and whether similar proportions of recovery can be expected for the two cognitive functions.

Methods: We assessed 35 patients with neglect and 14 patients with aphasia at 3 weeks and 3 months after stroke using standardized tests. Recovery patterns were classified with hierarchical clustering and the proportion of recovery was estimated from initial impairment using a linear regression analysis.

Results: Patients were reliably clustered into two different groups. For patients in the first cluster (N = 40) recovery followed a linear model where improvement was proportional to initial impairment and achieved 71% of maximal possible recovery for both cognitive deficits. Patients in the second cluster (N = 9) exhibited poor recovery (<25% of initial impairment).

Conclusions: Our findings indicate that improvement from neglect or aphasia after stroke shows the same dichotomy and proportionality as observed in motor recovery. This is suggestive of common underlying principles of plasticity, which apply to motor and cognitive functions.

1. Introduction

Evolution of motor function during the first 3 to 6 months after stroke is stereotypically bifurcated, consisting of either recovery to about 70% of initial impairment or of little to no improvement [1, 2]. This finding has enabled important insights on mechanisms of motor recovery [3-5]. Similarly, recovery from aphasia has also been shown to be proportional to initial aphasia severity, with an expected recovery of 70% of initial impairment [6]. However, it is not clear whether recovery from cognitive deficits also shows two strictly different paths as motor recovery or, rather, forms a continuum of improvements. Furthermore, it is unknown whether the rule of 70% improvement generalizes to recovery from left visuospatial neglect. The objective of this study was to investigate whether recovery from visuospatial neglect and aphasia after stroke shows similar characteristics as motor recovery.

2. Methods

We examined patients with first stroke presenting with left visuospatial neglect (35 patients; age 64±14 years; 17 women) or aphasia (14 patients; age 56±11 years; 6 women) after having obtained written informed consent. The study was approved by the local Ethical Committee. Patients were recruited from an inpatient neurorehabilitation unit. Inclusion criteria were the presence of a first stroke leading to neglect or aphasia. Exclusion criteria were the presence of other neurological disorders, disorders of vigilance or confusion limiting clinical testing. Neglect was defined in the initial examination as pathological result in at least one paper-and-pencil test (Bells or letter cancellation: $N \geq 3$ omissions on the left side; line bisection: ≥ 2 SDs right bias as compared to healthy controls) and the presence of clinically relevant signs of neglect in dressing and grooming or displacement. The initial clinical assessment was obtained at 3 weeks (T0) and a control assessment was performed at 3 months (T1) after stroke.

Neglect recovery was assessed with a letter cancellation test, which has shown great sensitivity for impairments of spatial exploration in previous studies [7]. Patients were asked to cross out inversed letters ‘T’ (N = 27 on each side of the sheet), dispersed among upright Ts. Neglect was quantified as the percentage of missed items on the left. An initial deficit of 100% corresponded to severe neglect, as the patient crossed out none of the items presented on the left side of the sheet.

Language was assessed with the Geneva Bedside Aphasia Score (GeBAS), including subscores for overall language function, production, and comprehension [8]. The type of aphasia was determined by an experienced speech therapist based on GeBAS scores and the Boston Group classification [9]. Four patients presented Broca aphasia, three global aphasia, two transcortical motor aphasia, two anomic aphasia, one conduction aphasia, two Wernicke aphasia. The severity of aphasia was quantified as the percentage of missed points in the GeBAS battery, with 100% indicating no correct item.

Clinical improvement for both functions was measured as the difference in percentage scores between T0 and T1 (with positive scores indicating improvement over time).

All patients received neglect or speech-language therapy, quantified as number of hours. Patients were attributed to different recovery groups based on hierarchical clustering [2] of clinical scores at T0 and T1 using nearest Euclidean distances and a maximum of two clusters. Analyses were performed with the Statistics Toolbox of Matlab (Mathworks Inc, Natwick, USA).

3. Results

Patients could be reliably divided into two different clusters of neglect and aphasia recovery as evidenced by a cophenetic correlation coefficient >0.75. For both cognitive deficits, the majority of recovery patterns followed a linear model where improvement was proportional to initial impairment (PROP; Figure 1; filled squares). A second cluster of patients (five patients with neglect and four patients with aphasia) exhibited poor, non-proportional recovery (POOR; Figure 1; unfilled circles).

We further performed a linear regression of the observed improvement against the initial impairment of patients in the PROP group. For neglect, this resulted in a slope of 0.84 and an offset of -12.5, indicating a predicted recovery of 71% of initial impairment. In the case of aphasia, the slope was 0.69 and the offset 0.8, which also leads to a predicted recovery of 71%. R-square scores showed that these models accounted for 76% (visuospatial attention) and 94% (language function) of the variance in recovery of PROP patients, respectively. Conversely, patients in the POOR group recovered <25% of initial language impairment and <5% of initial neglect.

The same principles were found for the sub-tests evaluating oral production and comprehension of language. Moreover, patients falling in the POOR cluster were the same in both domains. The regression model fitted to PROP patients predicted an improvement of 65% of initial impairment for production and 94% for comprehension.

To further validate the separation into two recovery groups, we computed model residuals as the difference between the improvements predicted by the proportional model and the observed improvement. These residuals corroborate that PROP (Figure 1; filled bars) and POOR patients (Figure 1; unfilled bars) follow two strictly separate recovery paths and do not form a continuum of distributed improvements.

Importantly, the amount of neglect and language therapy given to PROP and POOR patients did not differ ($p>0.68$, Mann-Whitney U test). Age ($p>0.4$, unpaired t-test), gender ($p=1$, Fisher's exact test), and lesion volume ($p>0.6$, Mann-Whitney U test) were also comparable between groups. The POOR group was not significantly associated with the presence of motor ($p>0.5$, Fisher's exact test) or visual field deficits ($p>0.1$, Fisher's exact test) at T0 in neglect and aphasia patients.

4. Discussion

Our study extends previous findings and indicates that recovery during the first months after stroke is guided by general principles underlying brain plasticity, which are common to motor and cognitive functions.

First, repair mechanisms seem to have an intrinsic capacity to recover about 70% of lost functions. The same proportion has been demonstrated in previous studies for motor [1-4] and language recovery [6] in PROP patients. The present study confirms the same rule for recovery from neglect. It should be noted, however, that our initial assessments were made somewhat late and did not capture the entire recovery period. We therefore may have underestimated the full proportion of recovery. On the other hand, the same proportion was found for language and motor function even when the initial assessment was obtained a few days after stroke onset [1, 2, 6]. It will be interesting in the future to examine the mechanisms underlying these proportions of expected recovery and possible specific treatments that may increase them.

Second, under some circumstances, the intrinsic repair mechanisms appear to remain inefficient in a subset of patients with severe affection. In the case of motor function, this occurs in patients with severe disruption of the cortico-spinal tract [3-5]. Here, we demonstrate the same dichotomy for aphasia and neglect. The occurrence of POOR was not significantly associated with age, gender, lesion volume, or concomitant motor or visual field deficits in our sample. We may have missed smaller differences in these variables due to a low sample size. However, it is likely that the recovery path is primarily influenced by other factors such as lesions to particular brain structures that need to be identified in future imaging studies.

The lack of significant differences in treatment duration between PROP and POOR patients confirms that the dichotomy was not biased by differences in therapy intensity. One might be tempted to further derive a general lack of efficacy of rehabilitation treatments from this observation. However, all patients in our sample underwent rehabilitation; therefore it is unknown whether a similar gradient of recovery would have been obtained without treatment. Yet, the existence of the POOR group suggests that some patients with severe affections currently do not sufficiently benefit from available treatments. It will be critical to identify the behavioral and physiological factors associated with poor recovery from neglect and aphasia in the future as this might help develop more effective treatments for this group in the future.

Interestingly, when looking at subdomains of language function, we find variations in the average proportion of recovery. This is in agreement with an earlier study [6], which also showed higher proportion of recovery for comprehension (83%), compared to naming (68%) and repetition (70%). Future studies on larger samples can further examine recovery patterns of specific language functions as well as the underlying mechanisms.

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Figure

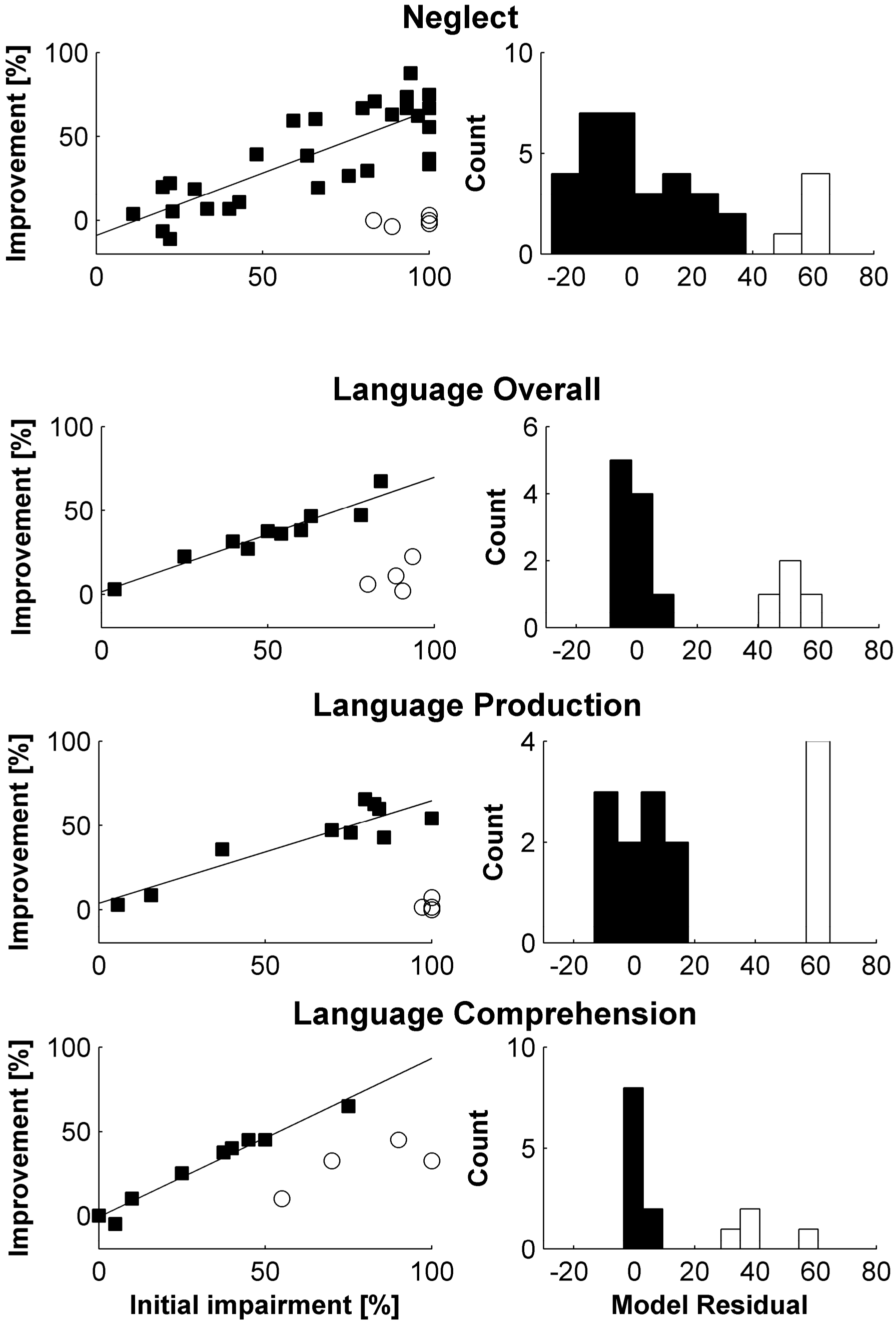

Figure 1. Recovery from neglect and aphasia after stroke followed one of two strictly different paths. Patients with filled squares recovered about 70% of their initial impairment (proportional recovery), while patients with empty circles showed no or very little improvement (left column). A histogram of the deviation from proportional recovery demonstrates the clear separation into two groups (right column).