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Research report

Time course of visuospatial neglect early after stroke: A longitudinal cohort study

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ABSTRACT

The aim of the current study was to investigate recovery of visuospatial neglect during the first year after stroke. Visuospatial neglect was measured using two frequently and widely used tests: the letter cancellation test (LCT) and the line bisection test (LBT). This was a prospective cohort study of 101 stroke patients. Of these 101 patients, 51 patients showed visuospatial neglect. All time-dependent measures were taken weekly, starting from within 14 days after stroke onset. From week 10–20 biweekly measurements were obtained. Follow-up measurements were performed at weeks 26, 38, and finally 52. For the present study, number of misses in the LCT, split on contralesional versus ipsilesional side, as well as the deviation from the actual midpoint in mm in the LBT were used. The longitudinal relationship of (bi)weekly time on improvement in LBT and LCT were investigated using random coefficient analysis and joinpoint analyses. Results indicated that progress of time is an independent covariate that reflects neurological recovery of visuospatial neglect. Additionally, trend changes were obtained in between 12 and 14 weeks post-stroke with respect to the neglected side. This is the first prospective cohort study in which the time course of neglect is investigated by using intensive serial measurements in the early months post-stroke.

1. Introduction

Visuospatial neglect, commonly referred to as neglect, is one of the most frequent disorders following stroke, involving about 25–30% of all patients (Appelros et al., 2002; Buxbaum et al., 2004). Patients with neglect show impaired or lost awareness for events and (visual, auditory, or tactile) stimuli located on the contralesional side of space (Halligan and Marshall, 1993; Heilman and Van Den Abell, 1980). It occurs for lesions to either hemisphere, but it is more severe and enduring after right hemisphere damage (Stone et al., 1993). The presence of neglect has been associated with poor motor recovery, higher disability, and poor responses to rehabilitation services (Katz et al., 1999; Cherney et al., 2001; Buxbaum

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et al., 2004; Nys et al., 2006). Although it is assumed that 'spontaneous' neurological recovery (i.e., early time-dependent changes immediate after stroke) can occur in the first weeks to months post-stroke, progress of time does not necessarily ameliorate visuospatial neglect in all patients (Kerkhoff, and Schenk, 2012). For example, it is known that visuospatial neglect can be found up to more than a year after a neurological incident (Karnath et al., 2011; Rengachary et al., 2011).

Unfortunately, proper prospective cohort studies in which the time course of neglect is intensively investigated are scarce. Only few studies associated neurological recovery of neglect with time (Cassidy et al., 1998; Farnè et al., 2004; Jehkonen et al., 2000, 2007; Levine et al., 1986; Rengachary et al., 2011; Samuelsson et al., 2003; Stone et al., 1992). All these studies reported very few serial measurements (ranging from 2 up to 7), making it impossible to carefully investigate the non-linear pattern of neurological recovery explained by progression of time post-stroke alone. Additionally, the initial measurement took place within the first 14 days in 3 studies (Cassidy et al., 1998; Jehkonen et al., 2000; Rengachary et al., 2011), making it impossible to measure the magnitude of neurological recovery within the first 8 weeks. In other words, the time course of recovery of neglect symptoms is rather unknown by lack of good prospective cohort studies that started early post-stroke with multiple serial measurements over time. In contrast to a fierce lack of understanding of the impact of time on severity of neglect, ample evidence exists for other clinical outcomes after stroke, such as impairments and disabilities of the upper (Feys et al., 1998; Goodwin and Sunderland, 2003; Sunderland et al., 1989) and lower paretic limb (Kollen et al., 2005; Kwakkel et al., 1999) as well as activities of daily living (Duncan et al., 1994). These studies with intensive serial measurements in time suggest that the time course of spontaneous neurological recovery follows a natural logistic pattern in which progress of time is statistically significant in the first 10–12 weeks post-stroke (Kwakkel et al., 2006).

The aim of the present study is to investigate the effects of progress of time post-stroke alone on reduction in visuospatial neglect up to 52 weeks post-stroke in an intensive repeated measurement design. For this aim we hypothesize that progress of time as a reflection of recovery of neglect without any specific treatment parallels recovery of other neurological impairments such as strength and synergism. In addition, we hypothesize that the process of time-dependent change is non-linear in time and statistically significant up till 12 weeks post-stroke. For this reason, differences in trends in the pattern of recovery of letter cancellation task (LCT) and line bisection task (LBT) will be investigated in the first year post-stroke. The current study will therefore allow for a more valid interpretation of how neurological recovery affects severity of neglect over time.

2. Methods

2.1. Participants

In this study, 101 patients with stroke participated with a mean age of 65 years [standard deviation (SD) = 12]. Data from these patients were published before (Kwakkel et al., 1999; Kollen et al., 2005). Patients were included when they met the following criteria: (1) aged between 30 and 80 years; (2) an ischaemic, first-ever, stroke, involving the medial or anterior cerebral artery as revealed by computer axial tomography (CAT) or magnetic resonance imaging (MRI); (3) an inability to walk at first assessment; (4) no complicating medical history such as cardiac, pulmonary, or orthopaedic disorders; (5) no severe deficits in communication, understanding, and memory; (6) written or verbal informed consent and sufficient motivation to participate. The Mini-Mental State Examination (MMSE; Folstein et al., 1975) was used to screen cognitive impairment and only patients with a score of >24 were included in the trial. A speech therapist assessed the ability to communicate and accepted a cut-off point of the 50th percentile corrected for age on the Dutch Foundation Aphasia Test (Deelman et al., 1981). Within 14 days post-stroke, patients were randomly assigned to a rehabilitation programme with emphasis on (1) arm training, (2) leg training, or (3) immobilization of the paretic arm and leg by an inflatable pressure splint (i.e., placebo condition; Svend Andersen, Haarlev, Denmark). The first two groups were assigned for arm or leg training, which was individually applied by local physical and occupational therapists, in addition to 15 min/day leg training, 15 min/day arm rehabilitation, and 1.5 h/week ADL training (activities of daily living) by an occupational therapist. The last group was schedule for immobilization of the paretic arm: a splint was applied with the patient's supine for 30 min 5 days/week. None of the patients received training to ameliorate visuospatial neglect (Kwakkel et al., 1999).

2.2. Procedure

The research protocol was implemented within 14 days after stroke onset. Final outcome was defined at 52 weeks after stroke. Each entire testing procedure took 45–75 min, depending on the level of disability. All functional measurements were performed by GK.

2.3. Outcome measures

As most improvements were expected to emerge in the first months post-stroke, weekly measurements were done during the initial 10 weeks, followed by biweekly measurements until the 20th week. Thereafter, follow-up measurements were performed at 26, 38 and 52 weeks. All outcome measures were obtained during these sessions.

The following primary and secondary outcome measures were evaluated:

1. A LBT (see Fig. 1, left panel), which involved indicating the centres of 10 lines, was applied to investigate the influence of time on bisecting performance, for both groups (neglect *vs* non-neglect) separately. The start of half of the lines was more towards the left of the centre of the page, the start of the other half was more towards the right of the centre of the page. The lines were presented on a sheet of A4 paper and were 10.7 cm each.
2. A LCT (see Fig. 1, right panel), which involved cancelling Os among other letters was applied to demonstrate presence