Neural plasticity and hemispatial neglect in stroke
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Abstract
The ability to outline the world and our place in it characterises our humanity. Stroke or brain injury can alter this world-making capability temporarily or permanently. The stroke patient’s world, once intelligible and practicable, is transformed into a confusing, unapproachable and hostile environment. The skills of intellect, sensation, awareness and movement, which are honed over the course of a lifetime and which so characterise our humanity are the very abilities most compromised by stroke. Stroke can rob people of the most basic way of interacting with the world. We will outline what is neglect and its mechanism in brain plasticity.

Keywords: Neglect, Stroke, Brain plasticity.

Introduction
Stroke is a common disorder that produces a major burden for society largely through long-lasting motor disability in survivors. Recent studies have broadened our understanding of the processes underlying the recovery of motor function after stroke.1-4

The specific abilities that will be lost or affected by a stroke depend on the extent of the brain damage and, most notably, where in the brain the stroke occurred. The brain is an incredibly complex organ, and each area within it has responsibility for a particular function or ability (functional specialisation). Each functionally specialised area is connected widely to operate goal-directed complex tasks (functional integration). Performance of specific task could be changed by stroke either due to a lesion in specific area or due to disconnection between that with others.

Unilateral Spatial Neglect (UN) is defined as the failure to report, respond or orient to novel or meaningful stimuli presented to the opposite side of a brain lesion, when this failure cannot be attributed to either sensory or motor defects.5 Survivors of right-hemisphere strokes may experience left-sided neglect. Stemming from visual field impairments, left-sided neglect causes the survivor of a right-hemisphere stroke to ‘forget’ or ‘ignore’ objects or people on their left side.

The prediction to be made, based on the functional imaging data, is that damage to superior parietal lobule (SPL) or the more dorsal system should yield a deficit in goal-directed spatial attentional orienting, whereas damage to the more ventral temporoparietal junction (TPJ) should result in a deficit associated with stimulus-driven attention capture.6-8 However, the neuropsychological literature on neglect does not clearly bear out this distinction. The neural correlates and its function related to neglect still remain largely in debate, as the nature of this phenomenon seems to be very complex. Spatial attention deficits are most commonly associated with damage to the inferior parietal lobe in general, which includes TPJ5,9 rather than to superior portions like SPL. A further complication is that lesions that involve SPL exclusively only rarely produce clinical evidence of neglect. Consistent with this, studies confirm that the critical region mediating hemispatial neglect is the territory of the middle cerebral artery; specifically the angular gyrus on the lateral surface of the inferior parietal lobule (IPL). Moreover, studies of patients who underwent precisely localised corticectomy for relief of epilepsy converge on the right IPL which is the crucial region. But, surprisingly, these findings themselves have come under scrutiny. In a number of very recent studies, the center of lesion overlap in a group of individuals with hemispatial neglect covered the right superior temporal gyrus (STG: Brodmann 22 and 42) and planumtemporale, with continuation into the insula and operculum and pre/postcentralgyri.10,11 However, in a recent study, transcranial magnetic stimulation (TMS) to the STG had no effect on performance on the landmark task commonly used to diagnose neglect (subjects decide whether a short line placed through a long line bisects it or not) nor on performance on a conjunctive visual search task, whereas TMS to the posterior parietal cortex did impair performance. A number of possible explanations

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for these site-of-lesions discrepancies arise, including differences in procedures and definitions of hemispatial neglect. However, the net result is that there is ongoing and vigorous debate about the regions giving rise to neglect and controlling hemispatial attention. There is a long history in the neglect literature showing that lesions to many different sites can give rise to neglect, including parietal cortex,\textsuperscript{12,13} frontal lobes,\textsuperscript{14} basal ganglia and the thalamus (pulvinar)\textsuperscript{11} and that the underlying temporoparieto-occipital white matter is also relevant.

A consequence of this conceptualisation, which goes back to Marcel Kinsbourne, is the prediction that disruption of an element of this distributed network will give rise to contralateral neglect and ipsilateral enhanced attention (a prediction for which we have direct experimental support in humans).\textsuperscript{15} A further prediction is that in the face of a lateralized lesion resulting in contralateral neglect, disruption of the undamaged hemisphere should lead to resolution of neglect (a prediction for which we have also support from animal and human studies).

Discussion

Stroke survivors live with their deficits an average of 7 years,\textsuperscript{16} producing an important impact at social, clinical and economic levels.

It is usually presented together with other symptoms, such as motor, somatosensory deficits\textsuperscript{17} and anosognosia.\textsuperscript{18} The summation of all these negative symptoms makes rehabilitation especially difficult.

The epidemiology of neglect has been poorly studied. The reported frequency varies from 13 to 81% of patients with a right hemisphere stroke.\textsuperscript{19} The most recent large-scale multi-centre study on neglect\textsuperscript{20} studied 1,281 consecutive patients. Neglect occurred in 43% of right hemisphere lesions (RHL) and 20% of the left hemisphere (LHL). At 3 months, it remained in 17% of RHL and 5% of LHL. This data points to a relevant fact for our study: neglect often resolves spontaneously, offering a natural model of stroke recovery.

The most relevant clinical factor of neglect is that it is an important predictor of poor overall and cognitive recovery,\textsuperscript{21} both in acute\textsuperscript{22} and chronic phases\textsuperscript{23} of stroke. Despite this well-known strong negative effect, some patients do regain independence while others take up considerable rehabilitation resources.\textsuperscript{24} Rehabilitation treatment for these patients is available\textsuperscript{25} and it has been described that effective neglect rehabilitation has a facilitating effect on the recovery of other stroke deficits such as hemiplegia. The significance of neglect as a major source of stroke-related long-term disabilities justifies further research efforts to develop tools for the appropriate assessment and treatment of this complex multi-factorial syndrome.

The modulatory therapeutic effects of TMS have already been proven with great results in other neurologic and psychiatric disorders such as depression, obsessive compulsive disorder (OCD), Parkinson’s, epilepsy, etc.\textsuperscript{26} In these cases, the stimulation protocol consists of several sessions per week lasting from 1 to 3 weeks. Oliveri et al. (2001) firstly observed transient decrease of magnitude of neglect by repetitive TMS (rTMS) on unaffected posterior intraparietal sulcus.\textsuperscript{27} Feasibility of the therapeutic use of rTMS was checked by Brighina et al. (2003) for the first time, performing a small pilot study with 3 patients with stroke and chronic neglect.\textsuperscript{28} They tested them 15 days prior to the treatment and the day treatment began, to assess their levels of impairment. Then they applied 2 weeks of treatment (one session every other day) and tested the patients both at the end of the treatment and 15 days after that. The 3 patients presented with very significant improvement in 3 different diagnostic tasks. Most importantly though, it was shown that the improvement remained practically unchanged 15 days after the intervention. Therapeutic use of rTMS in neglect patient is based on an influential proposal about the mechanism contributing to neglect, “hemispheric rivary or competition theory.”\textsuperscript{29,30} Left hemisphere structures tend to shift attention and spatial behaviour rightwards, but analogous activation of right hemisphere structures tend to oppose or counterbalance this. Koch et al. (2008) hypothesised that the intact left hemisphere may become hyperexcitable after RHL, due to the release of inhibition from the damaged hemisphere, which was the case in neglect patients showing increased excitability of the circuit between posterior parietal cortex and primary motor cortex in the left hemisphere that was normalised by 1Hz rTMS over left posterior parietal cortex.\textsuperscript{31} Recently, new protocol called continous theta-burst stimulation was proven to have similar effects.\textsuperscript{32}

More accurate and complete studies are needed to confirm the therapeutic use of TMS in the recovery of post-stroke neglect, but available data are remarkably promising.

More importantly, it offers a potential for the development of new therapeutic interventions capable of inducing reparatory changes leading to functional recovery. Neglect is a well-suited disorder for the study of these general mechanisms. Stroke recovery research has been focusing on motor deficits, and no work has been...
done to date on neglect, specially in Middle East. The high incidence of natural neglect recovery though, the offers a natural model of post-stroke plastic reparatory changes. In addition, neglect is an important negative prognostic factor for general stroke recovery, and its rehabilitation has been shown to facilitate the recovery of other stroke deficits such as hemiplegia. This makes neglect recovery especially relevant clinically.

**Conclusion**

Small studies in the field of cognitive neuroscience have shown that TMS can induce significant neglect recovery, but translational and clinical research needs to be conducted in order to study its potential role as a therapeutic tool.

**Reference**