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# Bridging the gap between clinical neuroscience and cognitive rehabilitation: The role of cognitive training, models of neuroplasticity and advanced neuroimaging in future brain injury rehabilitation

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**Abstract**.
**BACKGROUND:** Magnetic resonance imaging (MRI) has brought about advances in the fields of brain plasticity and lifespan brain change, that might be of special interest for cognitive rehabilitation research and, eventually, in clinical practice. Parallel, intensive cognitive training studies show promising results for the prospect of retraining some of the impaired functioning following acquired brain injury.
**OBJECTIVES:** However, cognitive training research is largely performed without concurrent assessments of brain structural change and reorganization, which could have addressed possible mechanisms of training-related neuroplasticity.
**METHODS:** Criticism of cognitive training studies is often focused on lack of ecologically valid, daily-living assessments of treatment effect, and on whether the applied cognitive measures overlap too much with the training exercises. Yet, the present paper takes another point of view, where the relevance of recent MRI research of brain plasticity to the field of cognitive rehabilitation is examined.
**RESULTS:** Arguably, treatment ought to be measured at the same level of the International Classification of Functioning, Disability and Health model, as it is targeting. In the case of cognitive training that will be the "body structure" and "body function" levels.
**CONCLUSIONS:** MRI has shown promise to detect macro- and microstructural activity-related changes in the brain following intensive training.

Keywords: Cognitive training, cognitive rehabilitation, brain plasticity, magnetic resonance imaging, diffusion tensor imaging, brain morphometry

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Recent advances within the field of magnetic resonance imaging (MRI) are likely to change our knowledge concerning brain injury impairments, recovery and rehabilitation in at least two important areas:

1) MRI might be used to monitor rehabilitation-induced brain plasticity processes, measuring treatment effects at a macro- and microstructural level while the patient is undergoing the intervention.
2) Detailed information from brain mapping studies will be available, and may link neural structures and networks closer to specific brain functions. In turn, this can better explain and clarify the relationship between lesions and their symptoms, especially in areas difficult to assess by traditional tests, like executive functions, personality and cognition-emotion interactions. Moreover, injury localization and size assessed by structural MRI (sMRI) may predict more reliable recovery trajectories.

Current brain injury rehabilitation guidelines are at large characterized by lack of efficient treatment for reinstatement of impaired brain structures and functions (for reviews, see Cicerone et al., 2000; Cicerone et al., 2005; Cicerone et al., 2011). Certainly, well-documented patient stories like the one of Henry Gustav Molaison (who until he passed away in 2008 foremost was known as H.M.), have shown that damage to particular brain structures may cause lifelong loss of cognitive function (Corkin, 2002; Corkin, Amaral, Gonzalez, Johnson, & Hyman, 1997). However, most cognitive functions are associated with large networks of brain areas, which might be partly anatomically overlapping (Alvarez & Emory, 2006; Ptak, 2012; Schlosser, Wagner, & Sauer, 2006) and functionally interlinked (e.g. Hester & Garavan, 2005). Unless an injury or ablation have harmed a highly critical structure, as in the special circumstances of Mr. Molaison, may cognitive functions prove to be – at least to some extent – adaptable to lesions? Recently, intensive post-injury cognitive training programs have shown promising results, both for attention and working memory (computerized cognitive training; Johansson & Tornmalm, 2012; Lebowitz, Dams-O'Connor, & Cantor, 2012; Lundqvist, Grundstrom, Samuelsson, & Ronnberg, 2010; Westerberg et al., 2007) and executive functions (e.g. Goal Management Training in combination with other interventions; for recent reviews, see Krasny-Pacini, Chevignard, & Evans, 2013; Manly & Murphy, 2012).

## 1. MRI based measures as an outcome measure of intensive training

The traditional measurements applied in cognitive rehabilitation, such as neuropsychological assessment, structured observation, clinical interviews and self-report questionnaire, do not provide specific information about what that happens at a brain structural level in response to treatment. In this sense the brain is still only a "black box" for which our only concern is what output (effect) that follow an input (treatment) (for reflextions on traditional behavioral psychology and the new brain sciences, see Skinner, 1989).

Clinical MRI is mainly based on radiologists' qualitative expert opinion regarding presence or absence of abnormalities in the brain images. Recent advances have made it possible to monitor neural irregularities not evident even to the trained eye (e.g. Grydeland et al., 2010), and MRI based techniques for quantifying sensitive regional volumetric and morphometric properties of the brain have been used in several studies investigating activity-induced brain plasticity processes. Draganski and colleagues showed that grey matter volume in task-relevant brain areas increased in response to intensive learning of a new skill (juggling) (Draganski et al., 2004). This finding has later been replicated and further explored by others (Driemeyer, Boyke, Gaser, Buchel, & May, 2008). Training-induced grey matter changes have later been found after learning of mnemonic techniques (Engvig et al., 2010), intensive studying (Draganski et al., 2006), and practice of a computerized spatial task (Haier, Karama, Leyba, & Jung, 2009). Further, substantial activity-dependent plasticity of white matter microstructure have been found (Fields, 2008; Scholz, Klein, Behrens, & Johansen-Berg, 2009), including following working memory training (Takeuchi et al., 2010) and learning of mnemonic techniques (Engvig et al., 2012). In relation to brain injury rehabilitation, data are limited, but one recent study using diffusion tensor imaging (DTI) found significant white matter changes in right arcuate fasciculus in patients with Broca's aphasia undergoing speech therapy (Schlaug, Marchina, & Norton, 2009), and a single case study showed white matter changes corresponding with computerized cognitive training phases following stroke (Nordvik et al., 2012). As illustrated by the latter two studies, advanced MRI based measures might be used as an outcome endpoint after brain injury rehabilitation interventions, in particular treatment targeting the "body structure" and the "body function"-levels of the International Classification of

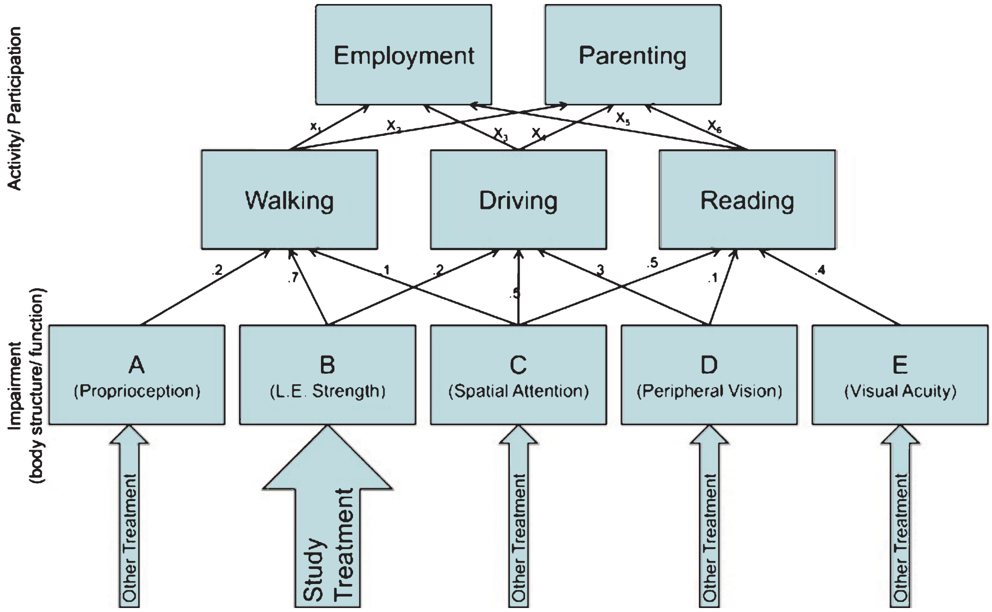


Fig. 1. For figure caption see the original article, Whyte and Barrett (2012). The digits next to the arrows represent a theoretical weighting of how much that factor contribute to the level above. Reprinted with permission from the publisher.

Functioning, Disability and Health (ICF) classification system (Stucki, 2005). Whyte and Barrett (2012) argue that interventions ought to be assessed at the same level as they are designed to target in the ICF-model. This suggests that for example activity training should be assessed by outcome measures developed for assessment of participation in and performance of activities, while cognitive training ought to be assessed at the body structure and function level. Transfer effects to higher and lower levels of the model is likely occur, however, the observable outcome of a specific intervention at a different level might be influenced also by other factors independent of the intervention (see Fig. 1; from Whyte & Barrett, 2012).

## 2. Prognostic predictions based on functional and structural brain mapping

A key postulate of brain injury rehabilitation is the notion of a close relationship between brain structures and brain functions. Even though the exact links between brain structural entities and neural activity, and cognitive and emotional properties are yet to large a mystery, MRI based methods show promise in disentangling some aspects of this relationship, and in the years to come the body of evidence is likely to be growing. Still, novel discoveries based on MRI methodology have already illustrated how prognostic predictions regarding cognitive impairments, can be made: Unilateral spatial neglect is a common cognitive sequelae after right-hemisphere stroke (Kleinman et al., 2008). Lesions in the parietal lobe are known to be associated with neglect (e.g. in the inferior parietal lobule; Ptak & Schnider, 2011), but which substructures within that region that is essential to visual attention have not been clear (Thiebaut de Schotten et al., 2012). Thiebaut de Schotten and colleagues (2012) combined information from a new DTI-based brain atlas of white matter pathways (Thiebaut de Schotten et al., 2011) with MRI data and neglect test results obtained from a sample of 58 right hemisphere stroke patients. The findings showed that lesions in one of the three branches of the superior longitudinal fasciculus (SLF) were the best predictors of left visual field neglect (see figure below).

The prevalence of unilateral spatial neglect is reported to increase with age in both genders, particularly from the age of 60 and onwards (Kleinman et al., 2008). This finding suggests a possible link between occurrence and the timing of a brain injury, and the severity of corresponding cognitive sequelae. Recently, MRI studies have brought about new knowledge about normal brain microstructural and cognitive development from early childhood and across lifespan (for a

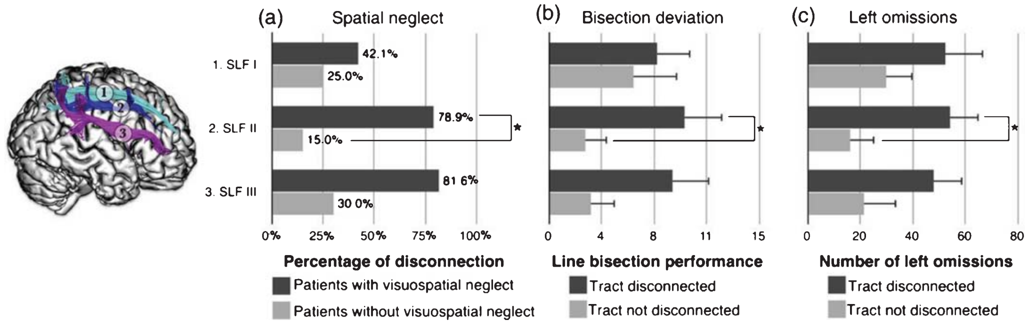


Fig. 2. For figure caption see the original article, Thiebaut de Schotten and colleagues (2012). Reprinted with permission from the publisher.

review, see Fjell & Walhovd, 2010). The exact interplay between brain developmental processes and acquired brain injury are still not fully understood. Knowledge derived from brain mapping studies of normal developing and aging brains may in the future help to predict how the timing of the injury (age of the patient) interacts with normal trajectories of brain structural and cognitive change (for recent review on neuroimaging and neurorehabilitation outcome in pediatric traumatic brain injury, see Wilde, Hunter, & Bigler, 2012).

The focus of cognitive rehabilitation ought to be the needs and the goals of the individual patient, and her/his family and social network. The diversity and complexity of injury-related issues in the life of patients seem to be best addressed with a comprehensive, holistic treatment approach. Hence, there are reasons for warning against a constricted focus only on impairment training in cognitive rehabilitation, like Barbara Wilson and colleagues do: "[R]ehabilitation has moved well beyond the drills and exercise approach. We no longer find it acceptable to sit people in front of a computer or workbook in the belief that such exercises will result in improved cognitive, and more important, social functioning" (p. 1; Wilson & Gracey, 2009). However, in light of the recent advances in neuroimaging studies of brain plasticity, it still might be that intensive, repetitive cognitive training, can play an important role in a comprehensive brain injury rehabilitation program, as recently recognized by Keith D. Cicerone in his Coulter Memorial Lecture (Cicerone, 2012). The appropriate measures of such training will, according to Whyte and Barrett (2012), be methodologies addressing the same level in the ICF model, i.e. body structure and body function. Advanced MRI offers the – until recently impossible – prospect of "*in vivo*" monitoring of treatment-induced neuroplasticity at a brain structural and functional level.

## Declaration of interest

All authors declare that they have no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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