Psychological Influence on the Effects of Cognitive Training in an Individual with Emotional Distress

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Abstract: Cognitive therapy can be an important part of a stroke survivor's rehabilitation but the effects of psychological factors on its training outcome is unclear. This study investigated the neuroplastic effects of working memory training on a single stroke survivor who has emotional distress due to prolonged motor impairment. The participant completed a sixweek auditory working memory training program at home. Neurocognitive tests and functional magnetic resonance imaging (fMRI) testing were conducted before and after training. Posttest neuroimaging results indicated increased neural efficiency for the trained task. However, there was no behavioral improvement on neurocognitive tests, and the participant's motivation declined as the training progressed. This case study indicated that while the performance of the trained task could be improved due to automaticity of task practice, psychological factors might play a key role in limiting the transfer of learning to other cognitive skills. Nevertheless, more research is needed to determine if these findings can be replicated in a similar clinical population.

Keywords: Stroke, working memory training, functional magnetic resonance imaging, emotional distress, motivation, neuroplasticity.

INTRODUCTION

Stroke is one of the leading causes of death and disability [1]. The type, size, and location of a stroke largely determine the damage inflicted to the physical brain structure and the deficits a person may experience. Many survivors require extensive rehabilitation to regain their physical and cognitive functions [1].

Cognitive training programs often use working memory paradigms as they have been shown to improve executive function [2]. Working memory is defined as the capacity to 'maintain' (store internally) and 'manipulate' (mentally process) online information for a short time [3-4]. Incoming information is typically viewed as either verbal or spatial in nature, but this research only considers the verbal category. This maintenance and manipulation of information is necessary for functional outcomes [5] and can ultimately influence a person's behavior [6]. For example, an efficient working memory is required in orderto successfully perform daily activities, such as recalling a phone number [5], and complex mental operations, like goal-directed behavior [6]. These types of deficitscan make participation in everyday life very challenging.

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Working memory rehabilitation programs have been shown to be effective in stroke survivors [2]. Westerberg et al. [7] placed stroke survivor participants into either a treatment or passive control group to assess the effectiveness of a working memory rehabilitation program. Participants in the treatment group received higher scores on non-trained tasks and perceived fewer cognitive problems after five weeks of training when compared to the control group. Another study analyzed the effects of two different styles of memory rehabilitation (process-orientated or strategy focused) against a control group that received only minimal cognitive treatment [8]. Most of the participants in the study had suffered a stroke, but some had other forms of organic brain damage. The authors found differences between the two treatment styles but both experimental groups performed better than the control participants. These studies demonstrate the value and benefits seen from working memory training.

However, the effects of cognitive training on stroke survivors who develop emotional distress have not been explored. Past studies have shown that emotional distress is common for people who had a stroke [9-10]. The most common manifestation is the presence of anxiety or depressive symptoms thatare not severe enough to be diagnosed as anxiety or depressive disorders [11]. Very often the presence of emotional distress is caused by an extended period of hospitalization, reduced physical mobility, uncertainty for future, and diminished social networks [12]. There has been evidence that a person's cognitive processing could be negatively influenced by emotional distress [13], which in turn would reduce the success of cognitive rehabilitation in stroke survivors. Nevertheless, the investigation of the impacts of emotional distress on neuroplasticity induced by cognitive training has received little attention.

Research using functional magnetic resonance imaging (fMRI) techniques can help explain complicated neural processes involved in cognitive activities. Neuroimaging studies on working memory have reported consistent activation in regions comprising the frontal-parietal network, including the inferior and middle frontal gyri, the superior and inferior parietal lobes, and subcortical structures such as the anterior cingulate gyrus, thalamus and caudate nucleus, which is independent of stimulus type [5, 14-16]. Multiple brain regions activate during the performance of working memory tasks [for a recent meta-analysis, please see 5 or 17], and many of these networks overlap [6]. Both left and right prefrontal cortices as well as the parietal regions in the brain show activation during verbal working memory tasks [3-5; also see reviews by 15 and 17]. Nevertheless, more research is needed to determine how components of a rehabilitation program affect damaged neural networks and cognitive outcomes [18].

This research uses a case-study design to investigate the neuroplastic effects of verbal working memory training on a client who has emotional distress due to motor impairments after stroke. The study will also explore the impacts of the client's motivation on the learning and skill transfer of functional tasks. The findings will help understand the impacts of psychological well-being on functional recovery.

METHOD

Case Demographics

The participant (EC) is a 38-year-old male who suffered a right-sided cerebral vascular accident (CVA) almost 19 years prior to the time of study (Figure 1). He completed post-secondary education and worked full time in central Alberta. EC is bilingual, right-handed, and has no documented history of any other neurological condition or mental illness. However, he has residual motor deficits that limit his left-hand movements. He is also concern about his body image because the spasticity in his left arm and fingers force his hand into an unnatural position. Despite his CVA occurring many years ago, EC continues to report working memory problems that are noticeable during work and home life.

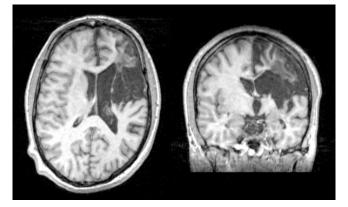


Figure 1: Structural scan showing the brain lesion of EC.

Procedure

EC was recruited through the out-patient clinic of a local hospital. He gave written consent for participating in the study during the intake interview at the laboratory. After that, he completed a battery of neurocognitive assessments to establish a record of current cognitive function in a variety of areas (e.g. working memory, inhibition, etc). The Cognitive Failures Questionnaire (CFQ) was also administered to measure EC's perception of his cognitive ability in daily activities. Following baseline assessment, EC was tested on verbal working memory n-back task using fMRI. EC then received a cognitive training program on a personal laptop that he took home for training. He repeated the assessment battery and fMRI scan within one week of completing the training program. The study was approved by the Health Research Ethics Boards of the University of Alberta Human Research Review Committee.

Neurocognitive and Functional Assessments

Arrow Task

This task assesses response inhibition abilities. A series of arrows (up or down) appear randomly on the screen during this computer task. The participant was required to make either a congruent (e.g. press 'up' on UP) or incongruent (e.g. press 'down' on UP) response using the directional keys for each trial. There were a total of 180 trials, organized in 10 blocks and each block contained 18 trials; 5 blocks were congruent condition and 5 blocks were incongruent conditions. Congruent blocks were presented followed bv incongruent blocks. For each trial, the arrow appeared for 100 ms, followed by 500 ms inter-stimulus interval. E-prime (version 2) was used to capture both accuracy and reaction time results. Both accuracy (correct response) and reaction time were recorded.

Cognitive Failures Questionnaire (CFQ)

The CFQ [19] is a self-report questionnaire that depicts a person's cognitive troubles during day-to-day activity. EC answered a variety of questions (e.g. Do you find you forget whether you've turned off a light?) and indicated on a 5-point Likert scale, from 0 (never) to 4 (very often), how often the statement applied to his performance. This form looks at activities involving memory, reasoning, and other aspects of cognition necessary for daily function.

Rehabilitation Therapy Engagement Scale (RTES-18)

At the end of training, EC rated on the RTES-18 to reflect his level of motivation in the training [20]. There are 18 items on the scale that address his perception on various aspects such as concentration, effort, and confidence. He indicated on a 4-point scale, from 0 (severely impaired) to 3 (meets potential), how he felt for each item.

Training Program

The training occurred five days per week over six weeks. Each day, EC completed four auditory working memory n-back tasks. The n-back task requires 'online' updating as each new stimulus on the screen becomes the new target, and the participant must constantly make comparisons between stimuli. This manipulation of actively retained information places demands on working memory processes [15]. During the task, EC monitored a series of auditory stimuli and pressed the spacebar on the computer keyboard when the current target was the same as a stimulus presented 'n' trials previously ('n' being an integer of 1, 2, or 3 typically please see Figure 2). Each task consisted of 10 blocks of trial (lasting 10 minutes); each block contained 30 trials; each trials consisted of 600 ms stimulus presentation and 1400 ms inter-stimulus interval (i.e., 1 minute per block). There were, on average, 5 targets per block. Stimuli were single digits from 1 to 9 (except 6 and 7) and letters from A to Z (except X, W, and Z). In the training, the 1-, 2- and 3-back tasks were randomly organized in advanceto vary the training schedule. For example, Day One may contain three 1back tasks and one 2-back task. In this way, EC always completed the same amount of training time (40 minutes per day) but the task difficulty varied. In total, EC completed 400 blocks for each of the 1-back, 2back, and 3-back tasks (i.e., 12,000 trials for each of the three types of tasks) during the six week period. The researchers were also able to ensure that EC

practiced a relatively equal number of stimuli and completed the training in a graded manner (i.e., more 3-back than 1- and 2-back tasks in the last two weeks of training).

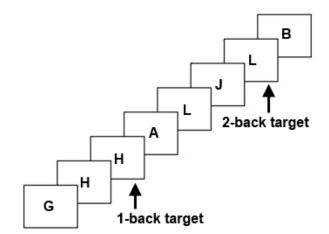


Figure 2: Diagram showing the n-back task. It shows examples of 1- and 2-back conditions.

fMRI Scanning

EC performed a series of n-back tasks during fMRI scanning before and after training. The tasks were the same as that he did in the training. During scanning, there were six runs of tasks with an equal number of 1and 2-back tasks. 3-back tasks were not included in the assessment as it was too difficult. The fMRI scanning was done at the Peter S. Allen MR Research Centre at the University of Alberta. A 1.5-T MRI system (Siemens) with a standard bird-cage head coil was used. Structural T1 weighted anatomical volumes were obtained before fMRI using SPGR (axial orientation, TR = 2080 ms, TE = 4.38 ms, FOV = 256 mm, slice thickness = 1 mm) for co-registration with the functional images. Functional imaging was performed to measure brain activation using the blood oxygenation leveldependent (BOLD) signal [21]. T2* functional images were obtained using EPI acquisition (TR = 1950 ms, TE = 40 ms, flip angle = 90° , FOV = 256 mm, effective acquisition matrix = 64×64). Each functional sequence consisted of 36 4-mm thick axial slices, positioned to image the whole brain.

The functional images were analyzed using the Statistical Parametric Map (SPM8) software package (Wellcome Department of Cognitive Neurology, Institute of Neurology, UK). Images underwent standardized preprocessing procedures including slice timing, motion correction, co-registration, normalization, and smoothing [16, 22]. The preprocessed data were modeled as a general linear model (GLM) with

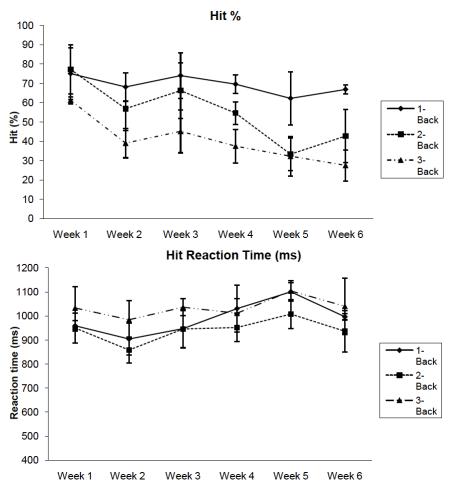


Figure 3: Two charts showing the hit percentages and reaction times accumulated over the six-week training period. All three conditions show decreased accuracy and speed of task performance over time. Error bars indicate standard deviations.

regressors representing the two experimental conditions, i.e., time (pre- versus post-) and memory load (1-back versus 2-back). Details of the analysis procedures could be found in Leung *et al.* [22] and Leung and Alain [16].

RESULTS

Performance of the Training Tasks

Overall, EC's performance declined over the sixweek period. There was a trend of decreasing hit rates and increasing reaction times in all the three tasks (1-, 2- and 3-back) from week 1 to 6 (Figure **3**).

Neurocognitive and Functional Assessments

There was a slight improvement in the performance of the arrow task (improved accuracy in the incongruent condition by 1.1%) (Table 1). However, EC showed no improvement on the CFQ (Table 1). He also showed comparatively low ratings in the RTES-18 with a total score of 24 out of 54 (Table 2).

Table 1: Results of Behavioral Performance in the Assessments

	Pre	Post
Arrow task – congruent condition		
Accuracy (%)	98.9	97.8
Reaction time (ms)	393.6	379.0
Arrow task – incongruent condition		
Accuracy (%)	98.9	100
Reaction time (ms)	441.6	453.3
CFQ		
Total score	37	44
1-back (during fMRI)		
Hit rate (%)	95.6	97.8
Reaction time (ms)	587.9	671.5
2-back (during fMRI)		
Hit rate (%)	97.8	100
Reaction time (ms)	768.4	723.9

 Table 2:
 Ratings on the 18 Items of the RTES-18 at the End of Training

Spontaneity1Enthusiasm0Concentration and focus1Interest in his rehabilitation program1Attentiveness to task demands2Motivation to participate in his recovery1Eagerness to learn2Effort put into therapy activities1Appropriate response to redirection2Ease of engaging in activities2Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals1Recognition of accomplishments2Tolerance for frustration0	RTES-18	Rating*
Concentration and focus1Interest in his rehabilitation program1Attentiveness to task demands2Motivation to participate in his recovery1Eagerness to learn2Effort put into therapy activities1Appropriate response to redirection2Ease of engaging in activities2Persistence and determination to face challenges1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Recognition of accomplishments2	Spontaneity	1
Interest in his rehabilitation program1Attentiveness to task demands2Motivation to participate in his recovery1Eagerness to learn2Effort put into therapy activities1Appropriate response to redirection2Ease of engaging in activities2Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals2	Enthusiasm	0
Attentiveness to task demands2Motivation to participate in his recovery1Eagerness to learn2Effort put into therapy activities1Appropriate response to redirection2Ease of engaging in activities2Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals2	Concentration and focus	1
Motivation to participate in his recovery1Eagerness to learn2Effort put into therapy activities1Appropriate response to redirection2Ease of engaging in activities2Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals2	Interest in his rehabilitation program	1
Eagerness to learn2Effort put into therapy activities1Appropriate response to redirection2Ease of engaging in activities2Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals2Recognition of accomplishments2	Attentiveness to task demands	2
Effort put into therapy activities1Appropriate response to redirection2Ease of engaging in activities2Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals1Recognition of accomplishments2	Motivation to participate in his recovery	1
Appropriate response to redirection2Ease of engaging in activities2Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals1Recognition of accomplishments2	Eagerness to learn	2
Ease of engaging in activities2Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals1Recognition of accomplishments2	Effort put into therapy activities	1
Persistence and determination to face challenges1Positive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals1Recognition of accomplishments2	Appropriate response to redirection	2
challengesPositive response to encouragement1Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals1Recognition of accomplishments2	Ease of engaging in activities	2
Understanding the benefits of therapy2Cooperation with therapist3Optimism and hope for recovery1Confidence or self-efficacy for reaching rehab goals1Recognition of accomplishments2		1
Cooperation with therapist 3 Optimism and hope for recovery 1 Confidence or self-efficacy for reaching rehab goals 1 Recognition of accomplishments 2	Positive response to encouragement	1
Optimism and hope for recovery 1 Confidence or self-efficacy for reaching rehab goals 1 Recognition of accomplishments 2	Understanding the benefits of therapy	2
Confidence or self-efficacy for reaching rehab goals1Recognition of accomplishments2	Cooperation with therapist	3
goals Recognition of accomplishments 2	Optimism and hope for recovery	1
	, ,	1
Tolerance for frustration 0	Recognition of accomplishments	2
	Tolerance for frustration	0

*0 = Major problem (Severely impaired); 1 = Minor problem (Mildly impaired); 2 = Could be better (Below potential); 3 = Optimal or ideal (Meets potential).

fMRI Results

There was a slight increase of hit rates (by 2.2% for both the 1-back and 2-back tasks). fMRI images showed activation of the frontal and parietal regions in the left hemisphere in the pre-training testing (Figure **4**). There was no significant activation in the right hemisphere where there was a large area of cortical damage resulting from his stroke. After training, the activations in the right hemisphere significantly subsided, leaving only activations in the temporal lobes for monitoring the verbal information.

DISCUSSION

EC's performance during the training period showed a remarkable pattern. His average accuracy for correct responses dropped consistently for all tasks (1, 2, and 3-back) each week. E.C.'s reaction time stayed relatively stable but showed a trend of decreasing speed even on the simple 1-back condition. Behavioral results from the pre- and post-training testing showed only slight positive change (between the ranges of

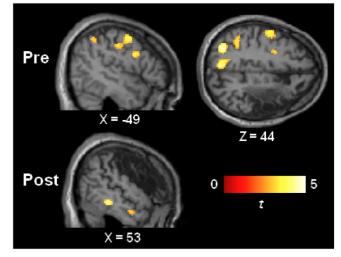


Figure 4: Activation maps showing significant activations in the pre- and post-training. The activation maps were computed from T contrasts (i.e., 2-back > 1-back). In the pre-training scan, both frontal and parietal activities were significantly activated in 2-back compared to 1-back tasks. In the post-training scan, activations at the frontal and parietal regions subsided, and activations at the temporal lobes were dominated in the 2-back compared to 1-back task.

1.1% to 2.2%) on the arrow task and the n-back tasks. The amount of change was not considered significant by comparison with previous studies (e.g., Leung *et al.*, [22]). His subjective perception of cognitive failure increased after training as reflected by the CFQ. He also gave low ratings on his efforts and frustration tolerance to the training as measured by the RTES-18.Taken together, the cognitive training did not appear to benefit EC on his cognitive and functional abilities.

Results from the post-test fMRI images reveal reduced activation in the frontal and parietal brain regions. The front and parietal regions are most active during working memory tasks [3-5]. The reduction of neural activation at these regions has been demonstrated in other neuroimaging research that investigates cognitive training effects [23]. Many previous studies have also found that practice appears to lower neural activity over time [17]. A decline in activation indicates a reduction of neural resources needed to perform the task and is often used as an indication of practice effect [23]. This practice effect appeared to happen in EC as he showed reduction of neural activities at the frontal and parietal regions. Previous studies have shown that transfer happens in tasks that share similar cognitive abilities such as working memory and response inhibition tasks [17]. Since both the working memory tasks (e.g., n-back) and response inhibition tasks (e.g., arrow task or stroop task) require neural activation of the fronto-parietal network and are core components of executive function

[25], transfer of skills between these tasks would be possible [17]. However, EC showed only very small extent of improvement on the arrow task and no improvement on subjective perception of cognitive skills. Hence, the transfer effect was not likely effective for him, and the reduced in neural activation at the frontal and parietal regions were likely related to the automaticity of task engagement due to repeated task practice.

The lack of training effects to other functional task performance could be explained by somepsychological factors. The most obvious factor is his motivation level and self-perceived confidence and efforts on the training tasks. From the RTES-18, it appears that EC has very low ratings of self-mastery over the training tasks. He does not feel confident with his performance and reports a low level of motivation throughout the training. Other possible factors might be that the training period is six weeks long, and the program requires an enormousamount of dedication to complete. By the last half of the training, EC could have lost interest to improve and simply fulfilled the training for completion's sake. Fatigue may have also played a role in his declining performance. Johasson and Tornmalm [24] found that many of their brain-injured participants found computer training "mentally exhausting". EC also tended to complete the tasks late at night so he may have had reduced concentration and attention. Lack of motivation and fatigue could cause EC to enter an "autopilot" mode and not fully engage with the task before him. A varying number of personal circumstances could also have played a part (e.g. stress at home or work, illness).

It is also worth noting that EC had a stroke almost nineteen years ago and continued to have a large area of damage over the right hemisphere involving the working memory network, i.e., the fronto-parietal neural network [15]. This may limit his ability to learn and transfer cognitive skills from one task to another. Therefore, the results of this study should be interpreted with caution. Future studies should consider increasing the sample size and including patients with similar demographic backgrounds and areas of the lesion to elucidate the effects of cognitive training.

CONCLUSION

This case study investigated the effects of working memory training on cognitive and functional improvements. The results indicated that while neural activation patterns showed evidence of improved neural efficiency on the trained task, the performance gain did not necessary transfer to other cognitive and functional task performance. The most plausible explanation is the psychological factors of the clients. Other factors like the post-injury duration, time-of-day of training and the extent of brain damage may also play a role in limiting the transfer of learning to other cognitive skills. More research is needed to determine if these findings can be replicated in a similar clinical population.

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REFERENCES

- [1] Public Health Agency of Canada. Tracking stroke and heart disease in Canada – Stroke highlights 2011. Ottawa, Canada. 2011. Retrieved from: http://www.phacaspc.gc.ca/cd-mc/cvd-mcv/sh-fs-2011/index-eng.php
- [2] Elliot MA. Efficacy of memory rehabilitation therapy: A metaanalysis of TBI and stroke cognitive rehabilitation literature. [unpublished dissertation]. Towson University, Maryland, USA 2013.
- [3] Philipose LE, Alphs H, Prabhakaran V, Hillis AE. Testing conclusions from functional imaging of working memory with data from acute stroke. Behav Neurol 2007; 18(1): 37-43. <u>http://dx.doi.org/10.1155/2007/396946</u>
- [4] Linden DE. The working memory networks of the human brain. Neuroscientist 2007; 13: 257–267. <u>http://dx.doi.org/10.1177/1073858406298480</u>
- [5] Wager TD, Smith EE. Neuroimaging studies of working memory: A meta-analysis. Cogn Affect Behav Neurosci 2003; 3(4): 255-274. http://dx.doi.org/10.3758/CABN.3.4.255
- [6] Westerberg H. Working memory: Development disorders and training. Karolinska University Press. Stockholm: Sweden 2004.
- [7] Westerberg H, Jacobaeus H, Hirvikoski T, et al. Computerized working memory training after stroke – A pilot study. Brain Injury 2007; 21: 21-9. <u>http://dx.doi.org/10.1080/02699050601148726</u>
- [8] Hildebrandt H, Bussmann-Mork B, Schwendemann G. Group therapy for memory impaired patients: A partial remediation is possible. J Neurol 2006; 253: 512-9. <u>http://dx.doi.org/10.1007/s00415-006-0013-6</u>
- [9] Hackett ML, Yapa C, Parag V, et al. Frequency of depression after stroke: A systematic review of observational studies. Stroke 2005; 36: 1330-40. http://dx.doi.org/10.1161/01.STR.0000165928.19135.35
- [10] White JH, Ghose S, Swindle RW. Predictors of depression and anxiety in community dwelling stroke survivors: A cohort study. Disabil Rehabil 2004; 36: 1875-982.
- [11] Schramke CJ, Stowe RM, Ratcliff G, et al.Poststroke depression and anxiety: Different assessment methods results in variations in incidence and severity estimates. J Clin Exp Neuropsyc 1998; 20: 723-37. http://dx.doi.org/10.1076/jcen.20.5.723.1117

- [12] Shimoda K, Robinson RG. Effect of anxiety disorder on impairment and recovery from stroke. J Neuropsych Clin N 1998; 10: 34-40. <u>http://dx.doi.org/10.1176/jnp.10.1.34</u>
- [13] Whiting DL, Deane FP, Simpson GK, McLeod HJ, Ciarrochi J. Cognitive and psychological flexibility after a traumatic brain injury and the implications for treatment in acceptancebased therapies: A conceptual review. Neuropsychol Rehabil 2015.
- [14] Nystrom LE, Braver TS, Sabb FW, Delgado MR, Noll DC, Cohen JD. Working memory for letters, shapes and locations: fMRI evidence against stimulus-based regional organization in human prefrontal cortex. Neuroimage 2000; 11: 424-46. http://dx.doi.org/10.1006/nimg.2000.0572
- [15] Owen AM, McMillan KM, Laird AR, Bullmore E. N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. Hum Brain Mapp 2005; 25: 46-59. http://dx.doi.org/10.1002/hbm.20131
- [16] Leung AWS, Alain C. Working memory load modulates the auditory "What" and "Where" neural networks. Neuroimage 2011; 55: 1260-9. <u>http://dx.doi.org/10.1016/j.neuroimage.2010.12.055</u>
- [17] Klingberg T. Training and plasticity of working memory. Trends Cogn Sci 2010; 14: 317-24. http://dx.doi.org/10.1016/j.tics.2010.05.002
- [18] Chen C, Wu C, Liao Y, *et al.* Working memory in patients with mild traumatic brain injury: Functional MR imaging analysis. Radiology 2012; 264: 844-51. <u>http://dx.doi.org/10.1148/radiol.12112154</u>

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- [19] Broadbent DE, Cooper PF, FitzGerald P, Parkes KR. The cognitive failures questionnaire (CFQ) and its correlates. Brit J Clin Psychol 1982; 21: 1-16. <u>http://dx.doi.org/10.1111/j.2044-8260.1982.tb01421.x</u>
- [20] Kortte 2007...
- [21] Ogawa S, Lee TM, Kay AR, Tank DW. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. Proc Natl Acad Sci USA 1990; 87: 9868-72. http://dx.doi.org/10.1073/pnas.87.24.9868
- [22] Leung AWS, Ng BPS, Yuen J, Dixon G, Kim ES. Neuroplastic changes after auditory working memory training in a patient surviving multiple strokes. J. Neurosci Rehabil 2014; 1: 1-22.
- Kelly AMC, Garavan H. Human functional neuroimaging of brain changes associated with practice. Cereb Cortex 2005; 15: 1089-102. <u>http://dx.doi.org/10.1093/cercor/bhi005</u>
- [24] Johansson B, Tornmalm M. Working memory training for patients with acquired brain injury: Effects in daily life. Scand J Occup Ther 2012; 19: 176-83. http://dx.doi.org/10.3109/11038128.2011.603352
- [25] Miyake A, Friedman N P, Emerson M J, Witzki A H, Howerter A, & Wager T D. The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. Cogn Psychol 2000; 41(1): 49-100. http://dx.doi.org/10.1006/cogp.1999.0734