Cognitive stimulation through mHealth-based program for patients with Alcohol Dependence Syndrome – a randomized controlled study

P Gamito[1], J Oliveira[1], P Lopes[1,2], R Brito[1], D Morais[1], S Rebelo[2], D Silva[2], C Caçôete[2], A Deus[2]

[1]COPELABS/Lusophone University
[1]EPCV/Lusophone University
Campo Grande, 376, 1749-024 Lisbon, PORTUGAL

[2]Novo Rumo Clinic. São João de Deus Institute,
Estrada do Telhal, Mem Martins, Sintra, PORTUGAL

{pedro.gamito, jorge.oliveira, diogo.morais}@ulusofona.pt,
{pjflopes, rodrigoreisbrito, sararebelo03, didifipaa, cristiana.cacoete}@gmail.com, alberto.deus@isjd.pt

[1]*labpsicom.ulusofona.pt*

ABSTRACT

Alcohol abuse can impact on general cognitive functioning and more particularly on frontal lobe functions. One option available to reduce this impact may rest on rehabilitation paradigms that include cognitive stimulation programmes. This paper reports on a randomized controlled study where two sample of patients with alcohol dependence syndrome where enrolled: 1) on a mHealth-based cognitive stimulation program (CSP) within alcohol dependence treatment (experimental group) and 2) on the alcohol dependence treatment without CSP (control group). The CSP mHealth applications consisted on a serial of serious games designed to stimulate frontal lobe functions. Assessment was conducted with the Mini-Mental State Examination and the Frontal Assessment Battery. After 10 stimulation sessions the experimental group evidenced a significant improvement on frontal-lobe functioning when compared with the control group. As expected, no differences on general cognitive functioning were found between groups.

1. INTRODUCTION

Alcohol abuse has been associated with significant morphological changes in the brain. Structural neuroimaging studies have shown that changes affect several areas of the grey matter and the white matter, with cortical atrophy and reductions of brain volume (Bjork et al, 2003; Gazdzinski et al, 2005; Sullivan et al, 2005). These changes are found frequently in the frontal lobes (Moselhy et al, 2001; De Bellis et al, 2005; Kubota et al, 2001), in particular in the parietal and temporal cortex and in the white matter adjacent to these regions (Sullivan et al, 1995, 1996), as well as in the hippocampus, in the basal ganglions, in the thalamus and in the cerebellum (Sullivan and Pfefferbaum, 2005; De Bellis et al, 2005) and in the corpus callosum (Schulte et al, 2005; Pfefferbaum et al, 2006). These changes – and in particular those of the frontal white and grey matter – are associated to the severity of alcohol consumption (Pfefferbaum et al, 1998; De Bruin et al, 2005; Cardenas et al, 2005; De Bellis et al, 2005; Gazdzinski et al, 2005). In fact, several studies have shown that alcohol-dependent patients exhibit enlarged brain ventricles and sulcus along with smaller white and grey matter. The increase in the cerebrospinal fluid and reduction of the corpus callosum, as well as changes in the prefrontal and orbitofrontal areas are associated with the duration of alcohol abuse, even after longer periods of abstinence post-alcohol abuse (Bechara et al, 2001; Kaufman and Levin, 2001).

These changes have a functional impact: they are associated to significant changes in the cerebral metabolism of the prefrontal cortex, as has been shown in studies using Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) (Adams et al, 1993, 1995; Volkow et al, 1997; Tutus et al, 1998; Gansler et al, 2000). Regarding neurotransmission, a more recent study using PET and addiction-specific GABA receptors showed reductions in the amount of neurotransmitters among alcohol addicts (Lingford-Hughes et al, 2005).

The consequences of these changes at the cognitive level have been shown also in a variety of studies, which indicate changes in visual-spatial abilities, psychomotor speed and frontal lobe functioning, particularly in executive functions that comprise several cognitive domains raging from working memory, attention, planning to decision-making and inhibitory control (Chan et al, 2008; Parsons, 1998; Sullivan et al, 2000). These changes in alcohol addicts are reflected at the level of learning, attention, long and short-term memory, abstraction, problem resolution, efficacy in information processing (Noel et al, 2005) and decision-making (Bechara et al, 2001).

On the other hand, abstinence from alcohol has been associated to important recovery in brain volume, which grows with length of abstinence periods, in particular during the first few months after alcohol consumption stops (Moselhy et al, 2001).

The effect of abstinence can be leveraged and enhanced by cognitive stimulation programmes (CSPs). For example, Yohman and colleagues (1988) compared the performance on neuropsychological tests of a) recovering alcoholics who engaged in twelve hours of memory stimulation exercises spread out over two weeks b) recovering alcoholics who engaged in problem resolution techniques with a similar schedule, c) recovering alcoholics who did not engage in any stimulation over two weeks, d) and a control group of non-alcoholics. All the recovering alcoholics groups performed worse than the non-alcoholics but, importantly, the recovering alcoholics performed better after participating in the two cognitive stimulation programmes tested. Goldstein and colleagues (2005) tested the efficacy of a five-session CSP programme with alcoholics in detox, and found improved performance on a battery of neuropsychological tests among participants who participated in the sessions, in contrast to controls.

Traditionally, CSP programmes are based on pencil-and-paper exercises. More recently, some researchers have been adopting computer-based interactive serious games (SGs) to increase motivation and adherence to the programmes (Edmans et al, 2007; Gamito et al, 2011). In particular, these CSPs have been tested on patients recovering from alcohol or substance-abuse (Fals-Stewart and Lam, 2010; Gamito et al, 2013; Grohman and Fals-Stewart, 2003). A study of Gamito and colleagues (2013) was conducted with the aim of comparing the efficacy on recovering the cognitive function of alcoholics in traditional pencil-and-paper CSP with that of a mobile device-based CSP based on the same exercises. Their preliminary data indicate that although there was a general trend for improvement (in particular in mental flexibility, attention, and visual-spatial capacity) in all groups, which can be attributed to abstinence, this effect was more pronounced in the mobile-based CSP group.

In the current study, we again assessed the efficacy of a mobile device-based CSP for the cognitive rehabilitation of recovering alcoholics. We focused on comparing its efficacy on the recovery of specific frontal lobe-based functions with that of general cognitive abilities. Because our CSP exercises follow the general standard for these exercises, which are based mostly on training attention, working memory, logical reasoning and attention, having been conceived initially for patients with acquired brain injuries, we expected that they would have a stronger impact on frontal lobe functioning than on general cognitive abilities.

2. METHOD

2.1 Sample

This study was based on a randomized controlled trial (RCT) design to test the effects of neuropsychological intervention through mHealth-based applications in patients with alcohol dependence syndrome. The required sample size was calculated *a priori* with Cohen's f effect size for F tests (Cohen, 1988). A total sample size of 40 patients was required for this trial in order to detect a medium effect size (.30; 1-β = .80; α = .05). The assignment of patients to each condition was performed using simple randomization. Figure 1 describes the flow of the participants between conditions.

Forty-two patients diagnosed with alcohol dependence syndrome (ADS) according to DSM-IV criteria (38 males, M*age* = 45.45 years, SD*age* = 10.31, 9 years of formal education, M = 9, SD = 3.72) were recruited upon entry into an alcohol rehabilitation programme at a private clinic consisting of a traditional medication-aided abstinence treatment with psychological assistance.

Only patients that scored higher than the cut-off values for their age on the Mini Mental Examination Test – MMSE (Folstein et al, 1975) and with no clinical scores on the Symptoms Checklist Revised - SCL-90-R (Derogatis, 1994) were included in the study. Patients continued their regular medication regimen consisting of anxiolytics, mostly Diazepam and Tiapride, which help minimize withdrawal symptoms, and vitamins. The assistant psychiatrist of each patient guaranteed the stability of the medication regimens throughout the program.

Patients with dependency from substances other than alcohol or with history of previous neurological disorders were excluded from the study. Patients were also screened for minimal computer literacy; no patients were excluded due to these criteria.

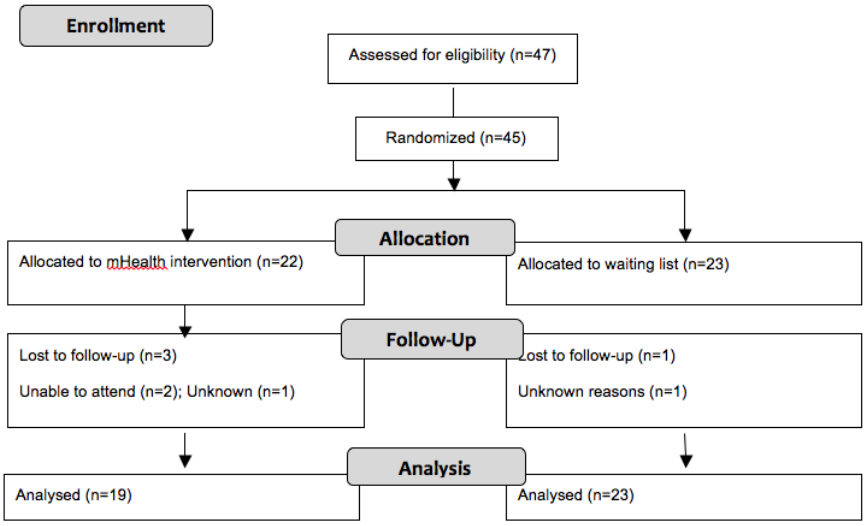

Figure 1. *Flow of the participants throughout the protocol.*

2.2 Measures

The following day after the first assessment, patients were tested on the first batch of a battery of neuropsychological tests and on the fourth day on the remainder of the battery. They were re-tested on the full battery at the end of the trial, a month later. For the current study we will focus only on two tests: the Mini-Mental State Examination (MMSE; Folstein et al, 1975) which measures general cognitive ability, and the Frontal Assessment Battery (FAB; Dubois, et al, 2000), which measures frontal-lobe functions.

2.3 Procedures

After the first testing, a randomly selected waiting list control group (n = 23, 22 males, M*age* = 48.61 years, SD*age* = 8.02, years of formal education, M = 9, SD = 3.68) simply continued following the traditional alcohol rehabilitation programme, a trial group (n = 19, 16 males and 3 females, Mage = 41.62yrs, SD*age* = 11.64, years of education, M = 8, SD = 3.84) also participated in a cognitive stimulation programme (CSPs) consisting of ten 45-50min sessions, twice or thrice a week for a month, starting from the sixth day of treatment, in which they played several serious games developed for Android and Windows (some of which were developed by this team, whilst others are available commercially) designed to stimulate in particular attention, memory and decision making, but also language, processing speed, strategic planning, perception, and spatial vision. At the end of the month of treatment all patients were re-tested on the full battery of neuropsychological tests. Prior to the initial screening, patients gave their written informed consent to the intervention. This trial was approved by the ethics committee of the host research institution.

The mobile cognitive stimulation program consisted of several mobile applications that were developed according to traditional paper-and-pencil rationales and originally conceived for cognitive stimulation on patients that had acquired cognitive impairments independently of the cause. Cognitive stimulation in each session comprised attention, working memory and logical reasoning exercises, which were standardized for all the patients in cognitive stimulation (see Table 1 for a more detailed description). The level of difficulty of each task increased progressively (i.e., one level at a time between sessions) throughout the cognitive stimulation rationale. In the last session, the same neuropsychological tests used in the first assessment were again applied. Two different teams of therapists were involved in recruitment, assessment and cognitive stimulation. A first group of therapists conducted patients' recruitment and assessments at baseline and follow-up. In the cognitive simulation sessions, an independent team of therapists provided the mobile devices with the exercises and supervised the sessions.

The hardware used to perform the exercises consisted of Samsung Galaxy 10.1" tablets. The applications (example shown in Figure 2) were developed using Unity 2.5 (Unity Technologies TM), and their alpha and beta versions had been previously tested by a group of students.

Table 1. *Cognitive Stimulation Program – Sessions and m-Health applications.*

Session1. Slot[4]/Memory[5]/Parking Zone[7]/Under pressure[8]/Snowflakes[2]
Session2. Slot[4]/Memory[5]/Under pressure[8]/Snowflakes[2]/Right order[3]
Session3. Slot[4]/Memory[5]/Hanoi Tower[6]/Snowflakes[2]/Right order[3]
Session4. Slot[4]/Memory[5]Odd-even[3]/Parking Zone[7]/Snowflakes[2]
Session5. Basket[3]/Odd-even[3]/Hand tricks[8]/Brick[1]/Memory[5]
Session6. Hanoi Tower[6]/Parking Zone[7]/Under pressure[8]/Memory[5]/Snowflakes[2]
Session7. Parking Zone[7]/Under pressure[8]/Selective transfer[4]/Memory[5]/Snowflakes[2]
Session8. Selective transfer[4]/Brick[1]/Hand tricks[8]/Memory[5]
Session9. Parking Zone[7]/Brick[1]/Hand tricks[8]/Memory[5]
Session10. Slot[4]/Memory[5]/Parking Zone[7]/Under pressure[8]/Snowflakes[2]

Note: Cognitive stimulation for [1]perception; [2]processing speed; [3]reasoning; [4]attention; [5]memory; [6]decision making; [7]planning; [8]spatial vision. These exercises are available online at (http://labpsicom.ulusofona.pt)

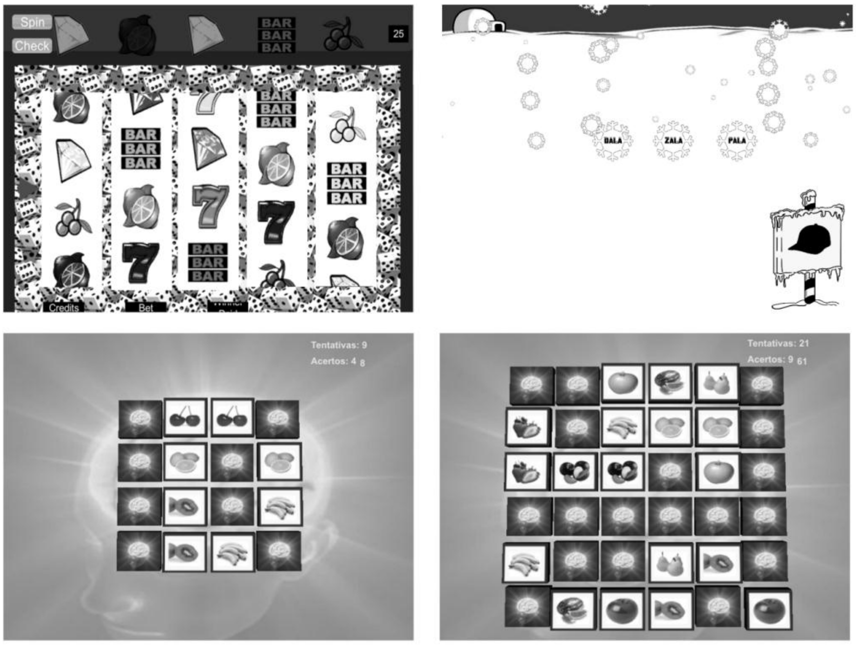

Figure 2. S*lot machine (top-left) for attention, visual memory task (bottom-left and bottom-right with increased difficulty) for working memory and the word-object correspondence (top-right) for logical reasoning.*

3. RESULTS

The dependent variables from the neuropsychological tests used for statistical analysis were the total scores of the MMSE and the FAB. The two groups did not differ in either gender or education, but given that there was a difference in age between groups (patients in the CPS group were significantly older than those in the waiting list control condition, $t(47) = 2.29$; $p = .027$), this variable was included as covariate in repeated measures Analysis of Covariance designs. Thus, two repeated measures ANCOVAs were performed for the total scores respectively of the MMSE and FAB with one within subjects' factor (baseline vs. follow-up), one between subjects' factor (i.e., group: m-Health cognitive stimulation vs. waiting list) and one covariate (i.e., age).

Results showed, as expected, no significant differences between groups on the MMSE, which measures general cognitive ability. The effects of age in this analysis were also non-significant ($p > .05$). On the other hand, the results of the FAB revealed a statistically significant interaction effect between factors ($F(1, 39) = 4.308$; $\eta2 = .099$; $p = .045$). This simple effects analyses for each group of the difference between baseline and follow-up showed that only the improvement in patients exposed to m-Health intervention was statistically

Proc. 10th Intl Conf. Disability, Virtual Reality & Associated Technologies
Gothenburg, Sweden, 2–4 Sept. 2014

significant ($F(1, 39) = 13.500$; $\eta2 = .257$; $p = .001$), indicating an improvement in frontal lobe functions following the m-Health intervention with virtual exercises, but not in the control group (Figure 3). No significant effects of the covariate were found in this analysis ($p > .05$).

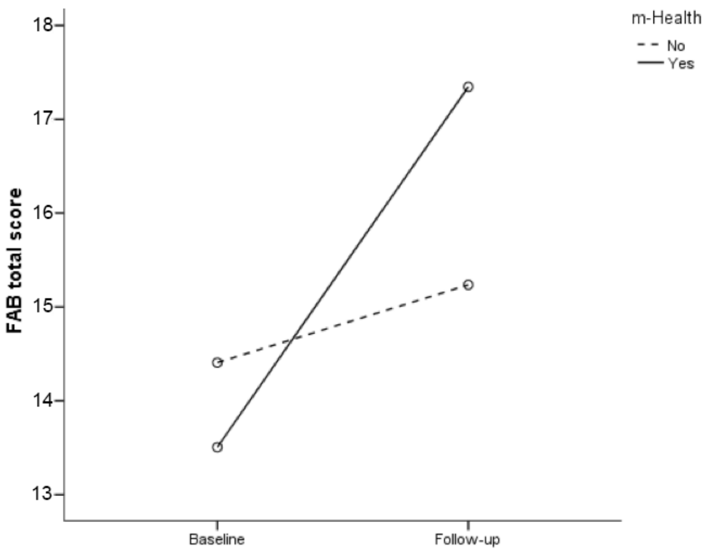

Figure 3. *Improvements in FAB scores at follow-up for m-Health group.*

4. DISCUSSION

As part of a wider dimension called executive functioning, the systematic and repetitive practice of tasks involving working memory and attention which our CSP programme involved, improved frontal lobe functioning significantly more than expected changes associated with spontaneous recovery rates in abstinent alcohol users in rehabilitation. Although our approach was developed for mobile technology to increase accessibility and frequency of cognitive training following its implementation in outpatient clinical populations, at this stage mobility and other related features were not tested. Thus, the improvements found cannot be attributed to these features, but rather to the benefits of stimulating systematically specific cognitive functions during recovery of alcohol dependence. Moreover, the advantage of this approach over traditional CSP, as reported in a previous study of Gamito and colleagues (2013), may be associated with the hedonic aspects of technology as key factors to increase motivation and engagement in the proposed exercises.

In the current study, we focused on comparing its efficacy on the recovery of specific frontal lobe-based functions with that of general cognitive abilities. Because our CSP exercises follow the general standard for these exercises, which are based mostly on training attention, working memory, logical reasoning and attention, having been conceived initially for patients with acquired brain injuries, we expected that they would have a stronger impact on frontal lobe functioning than on general cognitive abilities. The results of neuropsychological assessment have confirmed this prediction. Moreover, this lack of significant differences in the neuropsychological screening may also be related to a ceiling effect because of our exclusion criteria (i.e., only patients with scores above the MMSE cut-off points were selected) that were considered to ensure that patients have the capacity to give their consent to intervention.

Overall, on the one hand, these data indicate a beneficial role of neuropsychological interventions on ADS patients, suggesting that the paths to improve brain function are not limited to substance abstinence, but can be enhanced with neuropsychological interventions (see Goldstein and colleagues, 2005). On the other hand, our results also suggest that training working memory and attention functions gradually and in a systematic manner with mobile technology may be of clinical interest (Gamito et al, 2011). This may be particularly important to improve frontal system functions (Gamito et al, 2013), which is crucial to promote the overall adjustment in these patients.

Acknowledgements: This study was carried out in collaboration with the alcohol rehabilitation unit of the Casa de Saúde do Telhal. We would like to acknowledge the collaboration of the student interns in running the study.

5. REFERENCES

Adams, KM, Gilman, S, Koeppe, RA, Kluin, K.J, Brunberg, JA, Dede, D, Berent, S, and Kroll, PD, (1993), Neuropsychological deficits are correlated with frontal hypometabolism in positron emission tomography studies of older alcoholic patients, *Alcohol Clin Exp Res*, **17**, pp. 205-210.

Adams, KM, Gilman, S, Koeppe, T, Kluin, L, Junck, L, Lohman, M, Johnson-Greene, D, Berent, S, Dede, D, and Kroll, P, (1995), Correlation of neuropsychological function with cerebral metabolic rate in subdivisions of the frontal lobes of older alcoholic patients measured with [18 F] Fluorodeoxiglucose and positron emission tomography, *Neuropsychology*, **9**, pp. 275-280.

Bechara, A, Dolan, S, Denburg, N, Hindes, A, Anderson, SW, and Nathan, PE, (2001), Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers, *Neuropsychologia*, **39**, pp. 376-389.

Bjork, JM, Grant, SJ, and Hommer, DW, (2003), Cross-sectional volumetric analysis of brain atrophy in alcohol dependence: effects of drinking history and comorbid substance use disorder, *Am J Psychiat*, **160**, *11*, pp. 2038-2045.

Cardenas, VA, Studholme, C, Meyerhoff, DJ, Song, E, and Weiner, MW, (2005), Chronic active heavy drinking and family history of problem drinking modulate regional brain tissue volumes, *Psychiat Res-Neuroim*, **138**, *2*, pp. 115-130.

Chan, RC, Shum, D, Toulopoulou, T, and Chen, EY, (2008), Assessment of executive functions: Review of instruments and identification of critical issues, *Arch Clin Neuropsychol*, **23**, *2*, pp. 201-216.

Cohen, J, (1988), Statistical Power Analysis for the Behavioral Sciences, 2nd Edition, Hillsdale: Lawrence Erlbaum.

De Bellis, MD, Narasimhan, A, Thatcher, DL, Keshavan, MS, Soloff, P, and Clark, DB, (2005), Prefrontal Cortex, Thalamus and Cerebellar Volumes in Adolescents and Young Adults with Adolescent Onset Alcohol Use Disorders and Co-Morbid Mental Disorders, *Alcohol Clin Exp Res*, **29,** *9*, pp. 1590-1600.

De Bruin, EA, Hulshoff, HE, Bijl, S, Schnack, HG, Fluitman, S, Böcker, KB. E, Kenemans, JL, Kahn, RS, and Verbaten, MN, (2005), Associations between alcohol intake and brain volumes in male and female moderate drinkers, *Alcohol Clin Exp Res*, **29**, pp. 625-663.

Derogatis, LR, (1994), *SCL-90-R: administration, scoring and procedures manual*. National Computer Systems, Inc., Minneapolis.

Dubois B, Slachevsky A, Litvan I, Pillon B, (2000), The FAB: a frontal assessment battery at bedside, Neurology, **55**, pp. 1621−1626.

Edmans, J, Gladman, J, Cobb, S, Sunderland, A, Pridmore, T, Hilton, D and Walker, M, (2007), Validity of a Virtual Environment for Stroke Rehabilitation, *Stroke*, **37,** pp. 2770-75.

Fals-Stewart, W and Lam, K, (2010), Computer-assisted cognitive rehabilitation or the treatment of patients with substance use disorders: A randomized clinical trial, *Exp Clin Psychopharm*, **18**, pp. 87-98.

Folstein MF, Folstein SE, and McHugh PR, (1975), Mini-mental state: a practical method for grading the cognitive state of patients for the clinician, *J Psychiatr Res*, **12,** pp. 189-198.

Gamito, P, Oliveira, J, Lopes, P, Morais, D, Brito, R, Saraiva, T, Bastos, M, Cristóvão, S, Caçoête, C, and Picareli, F, (2013), Assessment of frontal brain functions in alcoholics following a health mobile cognitive stimulation approach, In *Annual Review of Cybertherapy and Telemedicine* (B.K. Wiederhold and G. Riva, Eds), **191**, pp. 110-114.

Gamito, P, Oliveira, J, Pacheco, J, Morais, D, Saraiva, T, Lacerda, R, Baptista, A, Santos, N, Soares, F, Gamito, L, and Rosa, P, (2011), Traumatic Brain Injury memory training: a Virtual Reality online solution. *Int J Disabil Hum De*, **10**, *2*, pp. 309-315.

Gansler, DA, Harris, GJ, Oscar-Berman, M, Streeter, C, Lewis, RF, Ahmed, I, and Achong, D, (2000), Hypoperfusion of inferior frontal brain regions in abstinent alcoholics: a pilot SPECT study, *J Stud Alcohol*, **61**, *1*, pp. 32-37.

Gazdzinski, S, Durazzo, TC, and Meyerhoff, DJ, (2005), Temporal dynamics and determinants of whole brain tissue volume changes during recovery from alcohol dependenc, *Drug Alcohol Depen*, **78**, *3*, pp. 263-273.

Goldstein, G, Haas, G, Shemansky, W, Barnett, B, and Salmon-Cox, S, (2005), Rehabilitation during alcohol detoxication in comorbid neuropsychiatric patients, *J Rehabil Res Dev*, **42**, pp. 225-234.

Grohman, K and Fals-Stewart, W, (2003), Computer-assisted cognitive rehabilitation with substance-abusing patients: Effects on treatment response, *J Cogn Rehabil*, **21**, pp. 2-9.

Kaufman, MJ, and Levin, JM, (2001), *Magnetic resonance findings in substance abuse*. Totowa: Humana Press.

Kubota, M, Nakazaki, S, Hirai, SS, Yamaura, A, and Kusaka, T, (2001), Alcohol consumption and frontal lobe shrinkage: study of 1432 non-alchoholic subjects, *J Neurol Neurosur Ps*, **71**, pp. 104-106.

Lingford-Hughes, AR, Wilson, SJ, Cunningham, VJ, Feeny, A, Stevenson, B, Brooks, DJ, and Nutt, DJ, (2005), GABA-benzodiazepine receptor function in alcohol dependence: a combined 11C-flumazenil PET and pharmacodynamic study, *Psychopharmacology*, **180**, pp. 595-606.

Moselhy, HF, Georgiou, G, and Kahn, A, (2001), Frontal lobe changes in alcoholism: a review of the literature, *Alcohol Alcoholism*, **36**, pp. 357–68.

Noel, X, Sferrazza, R, Linden, MVD, Acremont, M, Colmant, M, Hanak, C, Pelc, I, et al, (2005), Cognitive biases toward alcohol-related words and executive deficits in polysubstance abusers with alcoholism, *Addiction*, **100**, pp. 1302-1309.

Parsons, OA, (1998), Neurocognitive defcits in alcoholics and social drinkers: a continuum?, *Alcohol Clin Exp Res*, **22**, *4*, pp. 954-961.

Pfefferbaum, A, Adalsteinsson, E, and Sullivan, EV, (2006), Dysmorphology and microstructural degradation of the corpus callosum: Interaction of age and alcoholism, *Neurobiol Aging*, **27**, pp. 994–1009.

Pfefferbaum, A, Sullivan, EV, Rosenbloom, MJ, Mathalon, DH, and Lim, KO, (1998), A controlled study of cortical gray matter and ventricular changes in alcoholic men over a 5-year interval, *Arch Gen Psychiat*, **55**, *10*, pp. 905-912.

Schulte, T, Sullivan, EV, Müller-Oehring, EM, Adalsteinsson, E, and Pfefferbaum, A, (2005), Corpus callosal microstructural integrity influences interhemispheric processing: a diffusion tensor imaging study, *Cereb Cortex*, **15**, pp. 1384-1392.

Sullivan, EV, Marsh, L, Mathalon, DH, Lim, KO, and Pfefferbaum, A, (1995), Anterior hippocampal volume deficits in nonamnesic, aging chronic alcoholics, *Alcohol Clin Exp Res*, **19**, *1*, pp. 110-122.

Sullivan, EV, Marsh, L, Mathalon, DH, Lim, KO, and Pfefferbaum, A, (1996), Relationship between alcohol withdrawal seizures and temporal lobe white matter volume deficits, *Alcohol Clin Exp Res*, **20**, 2, pp. 348-354.

Sullivan, EV, and Pfefferbaum, A, (2005), Neurocircuitry in alcoholism: A substrate of disruption and repair, *Psychopharmacology*, **180**, pp. 583–594.

Sullivan, EV, Rosenbloom, MJ, and Pfefferbaum, A, (2000), Pattern of motor and cognitive deficits in detoxified alcoholic men, *Alcohol Clin Exp Res*, **24**, *5*, pp. 611-621.

Tutus, A, Kugu, N, Sofuoglu, S, Nardali, M, Simsek, A, Karaaslan, F, and Gonul, AS, (1998), Transient frontal hypoperfusion in Tc-99m hexamethylpropyleneamineoxime single photon emission computed tomography imaging during alcohol withdrawal, *Biol Psychiat*, **43**, pp. 923-928.

Volkow, ND, Wang, GJ, Fowler, JS, Logan, J, Gatley, SJ, Hitzemann, R, Chen, AD, and Pappas, N, (1997), Decreased striatal responsivity in detoxified cocaine abusers, *Nature*, **386**, pp. 830-833.

Yohman, TR, Schaeffer, KW, and Parsons, OA, (1988), Cognitive Training in Alcoholic Men, *J Consult Clin Psych*, **56**, *1*, pp. 67-72.