antipsychotic properties, and previous studies examining THC and CBD separately have found opposite effects on brain function [1]. Our primary aims were to determine (1) whether THC and CBD, alone and in combination affect brain function during rest and (2) whether these effects are differentially affected by cannabis use status.

Methods: In a double-blind, cross-over, placebo-controlled study, 15 frequent cannabis users (FREQ) and 15 infrequent users/nonuser controls (INFREQ) completed 5 randomised drug sessions with one week washout: (a) Placebo (vehicle); (b) THC 8 mg; (c) CBD 400 mg; (d) THC 8 mg + CBD 4 mg [LoCBD+THC]; (e) THC 12 mg + CBD 400 mg [HiCBD+THC]. Drugs were dissolved in 100% ethanol and vaporised using a Volcano® Vaporiser [2]. Electroencephalogram (EEG) was recorded using 32 channels across the scalp during 5 minutes of rest (eyes opened) before and after drug administration. EEG power was calculated for the following frequency bands: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), gamma1 (30–45 Hz), and gamma2 (55–90 Hz) in frontal, central and parietal regions for the left, middle and right side of the head. Data were log transformed and z-scored based on session for each site and frequency band and baseline corrected by subtracting data before drug administration from data after drug administration. Baseline corrected data were subjected to repeated-measures ANOVAs to examine drug condition effects for each frequency band separately. Only main effects of drug or group are reported below.

Results: Relative to placebo, THC increased EEG power in alpha, beta, gamma1 and gamma2 frequency bands, while CBD increased power in the gamma1 band, with a trend toward increased beta and gamma2 power. The increase in power with THC was greater than that for CBD in alpha, beta, gamma1 and gamma2, whereas THC decreased power compared to CBD in the theta band. LoCBD+THC decreased beta and gamma1 power compared to THC, while HiCBD+THC decreased beta, gamma1, and gamma2 power relative to THC. FREQ users showed decreased alpha power and a trend toward decreased theta power compared to INFREQ users during placebo administration. Decreased alpha power was also evident in FREQ compared to INFREQ during THC and CBD administration. There were no group differences in the combined CBD+THC conditions.

Conclusion: Acute THC, and to a lesser extent CBD, administration increased EEG power during rest. Combining CBD at both low and high doses with THC decreased EEG power, indicating that the combination of CBD and THC may normalise resting state brain function. The reduced alpha power at rest in FREQ users relative to INFREQ users during placebo, THC and to a lesser extent CBD, indicates that chronic cannabis use is associated with altered brain function and also that it changes responsivity to acute cannabinoids. This study extends current knowledge about the impact of THC, and importantly CBD on resting state brain function in frequent and infrequent cannabis users.

References

[1] Bhattacharyya et al., 2010. Opposite effects of delta-9-tetrahydrocannabinol and cannabidiol on human brain function and psychopathology. Neuropsychopharm 35, 764–74.
[2] Solowij et al., 2014. A protocol for the delivery of cannabidiol (CBD) and combined CBD and Δ9-tetrahydrocannabinol (THC) by vaporisation. BMC Pharmacol Toxicol 15, 58.

P.6.d.019 Cannabinoid hyperemesis syndrome; a prevalence study

P. Bruguera[1]*, L. Miquel[1], H. López-Pelayo[1], M. Balcells-Oliveró[1] [1]*Hospital clinic Institut de Neurociències, Psiquiatria. Unitat d'addiccions, Barcelona, Spain*

Introduction: Cannabis is the illegal drug most used in Europe. Despite its fame of being a soft drug, cannabis use has been related to many health problems. Cannabinoid hyperemesis syndrome (CSH) is a clinical condition present among some chronic cannabis users consisting in cyclic episodes of nausea and vomiting associated to compulsive bathing behaviour usually accompanied by abdominal pain. Despite prokinetic effects of cannabis by stimulating CB1 receptors in central nervous system, in some patients cannabis use produces contrary effects. This is explained by predominant effects of CB1 receptors on digestive tract, which reduces gastric motility, diminishes digestive secretions, and decreases contractility of lower esophageal sphincter. First defined in 2004 in Australia, epidemiology and ethiopathogenesis of this syndrome remains unclear.

Objective: To determine the prevalence of CHS in a drug dependent outpatient unit.

Method: A cross-sectional study was developed to determine the prevalence of CHS. All patients over 18 years old attended at the Cannabis Program at the Addiction Unit from Hospital Clínic de Barcelona since February to April 2014 were interviewed. From the 35 candidates, 22 (65.7%) patients were interviewed after signing informed consent, 1 (0.02%) could not sign the consent because of cognitive disability so was excluded, and 12 (34.3%) rejected to participate. A survey was designed to collect sociodemographic, clinic and diagnostic information about CSH. Psychiatric diagnoses were given according to DSM-V criteria.

Results: From the patients who answered the survey 12 (54%) were men, 19 (86%) were singles and 2 (22.7%) had university education.

In our sample we found a high proportion of psychiatric comorbidity (59%), 3 (13.6%) patients diagnosed with bipolar disorders, 8 (36.5%) with psychotic disorders and 2 (9%) with mixed anxiety depressive disorders.

All patients who answered the questionnaire presented at some point a cannabis use disorder. 18.2% (4) achieved abstinence during the last year, while 81.8% (18) maintained an active consumption of 2.1 joints per day on average.

18.2% (4) presented symptoms suggestive of CHS, partially (9.1% (2)) or the complete triad (9.1% (2)). Clients who presented the whole syndrome, experimented a clinical relieve with hot-showers. Only one of the patients with CHS linked cannabis use to the symptoms. 3 (75%) from the patients consulted to a physician, and were subjected to diagnosis procedures.

Conclusions: According to the results of our survey, Cannabinoid hyperemesis syndrome is an underdiagnosed clinical condition with a prevalence that could reach up to 18% in some special populations.

This syndrome produces high grade of discomfort, misdiagnoses and many unnecessary appointments to the medical specialist that could be avoided by exploring substance abuse disorders.

It should be suspected in emergency and digestive departments in patient with cyclic vomiting syndrome with an unknown cause.

References

[1] European Monitoring Centre for Drugs. 2012. Characteristics of frequent and high risk cannabis users.

[2] Pertwee, R.G., 1997 Pharmacology of cannabinoid CB1 and CB2 receptors. Pharmacol. Ther. 74,129–80.
[3] Allen, J.H., de Moore, G.M., Heddle, R., Twartz, J.C., 2004 Cannabinoid hyperemesis: cyclical hyperemesis in association with chronic cannabis abuse. Gut. 53,1566–70.
[4] Roca-Pallín, J.M., López-Pelayo, H., Sugranyes, G., Balcells-Oliveró, M.M., 2013 Cannabinoid hyperemesis syndrome. CNS Neurosci. Ther. 19, 994–5.
[5] Simonetto, D.A., Oxentenko, A.S., Herman, M.L., Szostek, J.H., 2012 Cannabinoid hyperemesis: a case series of 98 patients. Mayo Clin. Proc. 87, 114–9.

P.6.d.020 Atomoxetine reduces attentional bias to cocaine-related cues irrespective of norepinephrine transporter gene polymorphism

C.H. Popham[1]*, M. Luijten[2], H. Ziauddeen[1,3], S.A.E. Brain[1], R. Regenthal[4], I.H. Franken[2], B.J. Sahakian[1,5], E.T. Bullmore[1,3,5,6], T.W. Robbins[1,5], K.E. Ersche[1,5] *[1]University of Cambridge, Department of Psychology – Psychiatry and Neurosciences, Cambridge, United Kingdom; [2]Erasmas University Rotterdam, Institute of Psychology, Rotterdam, The Netherlands; [3]Cambridge and Peterborough NHS Foundation Trust, Department of Psychiatry, Cambridge, United Kingdom; [4]University of Leipzig, Division of Clinical Pharmacology – Rudolf-Boehm-Institute of Pharmacology, Leipzig, Germany; [5]University of Cambridge, Behavioural and Clinical Neuroscience Institute, Cambridge, United Kingdom; [6]GlaxoSmithKline, Clinical Unit Cambridge, Cambridge, United Kingdom*

Introduction: Addiction to cocaine is a major public health problem with a pressing need to improve treatment. Drug users' attention to drug-related cues, which are known to trigger drug-taking, could present a potential target for treatment interventions [1]. The pharmaceutical agent atomoxetine, which inhibits the reuptake of noradrenaline in the brain by blocking the noradrenaline transporter (NET), may have therapeutic potential for improving attentional control in drug addiction. Converging evidence from studies in humans and animals have shown that atomoxetine improves inhibitory control [2] and reduces relapse following drug abstinence [3], but clinical trials investigating its efficacy in reducing cocaine use in currently cocaine-dependent individuals (CDIs) have been less promising [4]. Faced with these disparate findings, we sought to explore the neurocognitive mechanisms underpinning the moderation of response to atomoxetine by a polymorphism in the SLC6A2 gene, which encodes the noradrenaline transporter.

Objective: The aim of this MRC-funded study (MR/J012084/1) was to investigate the potential of atomoxetine to increase executive control over biased attention towards drug-related cues in CDIs. We hypothesized that efficacy of atomoxetine in improving attentional control is modulated by genotype.

Methods: In a double-blind, placebo-controlled, cross-over design, CDIs (N = 28) and healthy volunteers (N = 28) received a single oral dose of 40 mg atomoxetine and placebo. Participants were matched for genotype at the rs36024 locus into minor homozygous (TT), heterozygous (CT) or major homozygous (CC). Attentional bias to drug-related cues was investigated by a pictorial line-counting paradigm which employed cocaine-related and neutral images. Participants were asked to press a key in response to the number of lines appearing in both conditions. Task performance was measured by the mean response time for line counting cocaine-related pictures relative to neutral pictures. To investigate whether the modulatory effects of atomoxetine are affected by participants' diagnosis and genotype, we used repeated-measures analysis of variance (ANOVA) with drug treatment (placebo, atomoxetine) and picture category (neutral, cocaine-related) as the two within-subject factors, and diagnosis (control, CDIs) and genotype (CC, CT, TT) as the two between-subject factors.

Results: CDIs demonstrated a significantly longer latency than control volunteers in correctly counting the lines on the pictures depicting cocaine-related objects or activities compared with their responses to neutral pictures (category-by-diagnosis interaction $F_{1,50} = 5.45$, $p = 0.023$). There was no significant main effect of drug ($F_{1,50} = 0.55$, $p = 0.461$) but a significant main effect of diagnosis ($F_{1,50} = 26.2$, $p < 0.001$) and a significant 3-way interaction of drug-by-category-by-diagnosis ($F_{1,50} = 4.71$, $p = 0.035$). No significant main effect of genotype ($F_{2,50} = 0.36$, $p = 0.698$) and no significant drug-by-genotype interactions ($F_{2,50} = 1.38$, $p = 0.261$) were found. Self-reported feelings of drug craving did not increase significantly after the task ($F_{1,25} = 1.83$, $p = 0.189$) and were not affected by atomoxetine ($F_{1,25} = 0.59$, $p = 0.449$).

Conclusion: This study provides evidence that attentional bias to cocaine-related cues can be reduced by atomoxetine in CDIs irrespective of genotype. As drug-related cues play an important role in the maintenance of drug addiction and increase the risk of relapse, our findings may highlight the potential of atomoxetine to be used as an adjunct treatment in clinical practice to support patients in their attempts to re-gain control over their drug use.

References

[1] Waters, A.J., Marhe, R., Franken, I.H., 2012. Attentional bias to drug cues is elevated before and during temptations to use heroin and cocaine. Psychopharmacology 219 (3), 909–921.
[2] Chamberlain, S.R., Muller, U., Blackwell, A.D., Clark, L., Robbins, T.W., Sahakian, B.J., 2006. Neurochemical modulation of response inhibition and probabilistic learning in human. Science 311(5762), 861–863.
[3] Economidou, D, Dalley, J.W., and Everitt, B.J., 2011. Selective norepinephrine reuptake inhibition by atomoxetine prevents cue-induced heroin and cocaine seeking. Biological Psychiatry 69 (3), 266–274.
[4] Walsh, S.L., Middleton, L.S., Wong, C.J., Nuzzo, P.A., Campbell, C.L., Rush, C.R., Lofwall, M.R., 2013. Atomoxetine does not alter cocaine use in cocaine dependent individuals: double blind randomized trial. Drug and Alcohol Dependence 130 (1–3), 150–157.

Disclosure statement: This research was funded by the Medical Research Council (MRC, Grant MR/J012084/1) and was jointly sponsored by the University of Cambridge and Cambridge University Hospitals NHS Foundation Trust. Large parts of the infrastructure were provided by the Behavioural and Clinical Neuroscience Institute, which is supported by a joint award from the Medical Research Council and Wellcome Trust (G00001354). H Ziauddeen is supported by the Bernard Wolfe Health Neuroscience Fund and K D Ersche received support from the MRC. B J Sahakian consults for Cambridge Cognition, Servier and Lundbeck. She holds a grant from Janssen/J&J and has share options in Cambridge Cognition. TWR consult for Cambridge Cognition, Lilly, Lundbeck and GlaxoSmithKline and also holds research grants from those companies. E T Bullmore is employed part-time by GlaxoSmithKline and part-time by the University of Cambridge he holds stock in GSK. None of the other authors have financial support to disclose. All the authors declare that they have no competing or potential conflicts of interest in relation to this work.