

Media Release: European College of Neuropsychopharmacology

Pathological gambling is associated with altered opioid system in the brain, and a reduced feeling of euphoria when compared to healthy volunteers.

Embargo until: 00.01 Sunday 19th October (Central European Summer Time)

Berlin, 19th October 2014 All humans have a natural opioid system in the brain. Now new research, presented at the ECNP Congress in Berlin, has found that the opioid system of pathological gamblers responds differently to those of normal healthy volunteers. The work was carried out by a group of UK researchers from London and Cambridge, and was funded by the Medical Research Council. This work is being presented at the European College of Neuropsychopharmacology congress in Berlin.

Gambling is a widespread behaviour with about 70% of the British population gambling occasionally. However in some individuals, gambling spirals out of control and takes on the features of an addiction – pathological gambling, also known as problem gambling. The 2007 British Gambling Prevalence Survey¹ estimated that 0.6% of UK adults have a problem with gambling, equivalent to approximately 300,000 people, which is around the total population of a town like Swansea. This condition has an estimated prevalence of 0.5–3% in Europe.

The researchers took 14 pathological gamblers and 15 healthy volunteers, and used PET scans (Positron Emission Tomography scans) to measure opioid receptor levels in the brains of the two groups. These receptors allow cell to cell communication – they are like a lock with the neurotransmitter or chemical, such as endogenous opioids called endorphins, acting like a key. The researchers found that there were no differences between the receptor levels in pathological gamblers and non-gamblers. This is different to addiction to alcohol, heroin or cocaine where increases are seen in opioid receptor levels.

All subjects were then given an amphetamine tablet which releases endorphins, which are natural opiates, in the brain and repeated the PET scan. Such a release – called an ‘endorphin rush’- is also thought to happen with alcohol or with exercise. The PET scan showed that the pathological gamblers released less endorphins than non-gambling volunteers and also that this was associated with the amphetamine inducing less euphoria as reported by the volunteers (using a self-rating questionnaire called the ‘Simplified version of the amphetamine interview rating scale’, or SAIRS).

As lead researcher Dr Inge Mick said:

““From our work, we can say two things. Firstly, the brains of pathological gamblers respond differently to this stimulation than the brains of healthy volunteers. And secondly, it seems that pathological gamblers just don’t get the same feeling of euphoria as do healthy volunteers. This may go some way to explaining why the gambling becomes an addiction”.

“This is the first PET imaging study to look at the involvement of the opioid system in pathological gambling, which is a behavioural addiction. Looking at previous work on other

addictions, such as alcoholism, we anticipated that pathological gamblers would have increased opiate receptors which we did not find, but we did find the expected blunted change in endogenous opioids from an amphetamine challenge. These findings suggest the involvement of the opioid system in pathological gambling and that it may differ from addiction to substances such as alcohol. We hope that in the long run this can help us to develop new approaches to treat pathological gambling”

Speaking on behalf of the ECNP, Professor Wim van den Brink (Amsterdam), Chair of the Scientific Committee for the Berlin Congress, said:

“At the moment, we find that treatment with opioid antagonists such as naltrexone and nalmefene seem to have a positive effect in the treatment of pathological gambling, and that the best results of these medications are obtained in those problem gamblers with a family history of alcohol dependence. But this report from Dr Mick and colleagues is interesting work, and if confirmed it could open doors to new treatment methods for pathological gamblers”.

ENDS

Notes for editors

Please mention the European College of Neuropsychopharmacology Congress
in any stories which result from this press release.

Contacts

For more information please contact Inge Mick, i.mick@imperial.ac.uk

Professor Wim van den Brink can be reached via w.vandenbrink@amc.uva.nl

ECNP Press Officer, Tom Parkhill, can be contacted via tom@parkhill.it or on +39 349 238 8191

This study was funded by the Medical Research Council- MRC G1002226.

Note 1 British Gambling Prevalence

Survey <http://web.archive.org/web/20091128000055/http://www.gamblingcommission.gov.uk/pdf/British%20Gambling%20Prevalence%20Survey%202007.pdf>

The ECNP is an independent scientific association dedicated to the science and treatment of disorders of the brain. It is the largest non-institutional supporter of applied and translational neuroscience research and education in Europe.

ECNP organises a wide range of scientific and educational activities, programmes and events across Europe, promoting the exchange of high-quality experimental and clinical research and fostering young scientists and clinicians.

The annual ECNP Congress takes place in Berlin from 18-21 October. It is Europe's premier scientific meeting for disease-oriented brain research, annually attracting between 5,000 and 8,000 neuroscientists, psychiatrists, neurologists and psychologists from around the world.

Website: www.ecnp.eu

Abstract

P.6.f.002 **Endogenous opioid release in pathological gamblers after an oral amphetamine challenge: a [11C]carfentanil PET study** I. Mick¹, J. Myers¹, P. Stokes², A. Colasanti², D. Erritzoe¹, R. Gunn³, L. Clark⁴, E.A.

Rabiner³, A. Lingford-Hughes¹, D. Nutt¹ *1Imperial College London, Centre for Neuropsychopharmacology, London, United Kingdom; 2King's College London, Institute of Psychiatry, London, United Kingdom; 3Imanova, Centre for Imaging Science, London, United Kingdom; 4University of Cambridge, Department of Psychology, Cambridge, United Kingdom*

Purpose of the study: Gambling is a widespread behaviour that around 70% of the British population engage in at least occasionally. In some individuals, gambling spirals out of control and takes on the features of an addiction – pathological gambling. This condition has an estimated prevalence of 0.5–3% in Europe. The importance of the opioid receptor system in addictions is being increasingly recognized. There is strong evidence from recent PET studies that the opioid system in drug dependent individuals differs from healthy non-dependent participants', in particular higher mu opioid receptor (MOR) levels have been reported in alcohol, cocaine and opiate dependence [1]. Consistent with higher levels is that opiate antagonists are effective treatments for addictions, including pathological gambling (PG) [2]. In this study we are testing the hypotheses that PG would be associated with higher MOR levels and blunted endogenous opioid release after an oral amphetamine challenge compared with healthy volunteers (HV). We applied our [11C]carfentanil PET imaging with oral amphetamine challenge protocol [3].

Methods: 15 male HV (2 smokers, mean age: 34.5) and 14 PG (3 smokers, mean age: 33.9) underwent two [11C]carfentanil PET scans, one before and one three hours after an oral endorphin releasing administration of 0.5 mg/kg of d-amphetamine. Subjective responses to the amphetamine challenge were measured using the simplified version of the amphetamine interview self-rated scale (SAIRS: euphoria, restlessness, alertness, anxiety). Pre- and post-amphetamine scanning data (%DBPND) was compared using paired t-tests. For correlations between regional BPND change (%DBPND) and changes in subjective amphetamine effects (Dscores), we used non-parametric Spearman correlations. All data was normally distributed as determined by visual inspection as well as using the Kolmogorov-Smirnov and Shapiro-Wilk tests for normality.

Results: There were no significant differences between HV and PG in baseline availability of MOR. In HV, the oral d-amphetamine challenge led to significant ($p < 0.05$) reductions in [11C]carfentanil BPND in 8/9 regions of interest; caudate (0.009), putamen (< 0.001), thalamus (< 0.001), cerebellum (0.001), frontal lobe (< 0.001), nucleus accumbens (0.004), anterior cingulate (< 0.001) and insula cortices (< 0.001). Mean %DBPND ranged between -7.5% (caudate) and -1.5% (amygdala). There were no increases in BPND observed. In PG, %DBPND ranged between -2.6% (thalamus) and +1.2% (insula). There was an increase in BPND in 5/9 ROI. Significant reductions were observed in the thalamus (0.036) and putamen (0.021). Changes in subjective amphetamine ratings were limited. In HV, the mean change in euphoria scores was +1.2 (SD) 1.4, max change: +3 and in PG, mean: +1.1 (SD) 0.9, max: +3. An exploratory analysis of the relationship between Dscores and regional %DBPND did not show any significant correlations in HV or PG.

Conclusions: Whilst no higher baseline MOR availability was evident in PG compared with HV, following the amphetamine challenge, blunted endogenous opioid release was seen in PG compared with HV suggesting opioid dysregulation. We were able to detect changes in [11C]carfentanil BPND indicating endogenous opioid release without participants experiencing the adverse 'high', as evidenced by the lack of significant changes in euphoria scores.

References [1] Williams T.M., Daghlian M.R., et al. 2007. Brain opioid receptor binding in early abstinence from opioid dependence: positron emission tomography study. *Br J Psychiatry* 191: 63–9. [2] Potenza, M.N. 2008. Review. The neurobiology of pathological gambling and drug addiction: an overview and new findings. *Philos Trans R Soc Lond B Biol Sci* 363(1507): 3181–3189. [3] Colasanti, A., Searle G.E., et al. 2012. Endogenous opioid release in the human brain reward system induced by acute amphetamine administration. *Biol Psychiatry* 72(5): 371–377.