

Supplementary materials

Recruitment

Abstinent subjects with alcohol dependence (EtOH, N=30), obese subjects (>30 Body Mass Index, BMI) with binge eating disorder (BED, N=30) and obese controls without BED (N=30) were recruited via community and university-based advertisements in the East Anglia region. Two age- and gender-matched healthy volunteers (HV) were recruited for each subject group via community and university-based advertisements in East Anglia. Abstinent methamphetamine dependent subjects (Meth, N=23) were also recruited from an inpatient rehabilitation center in Eden Prairie, Minnesota, USA. Twenty age-matched HV were recruited from community advertisements in Minneapolis. Additional age- and gender-matched HV were recruited from community advertisements in East Anglia such that there were 2 healthy volunteers per Meth subject. For all patient groups primary diagnoses were confirmed by a psychiatrist using the Diagnostic and Statistical Manual of Mental Disorders, Version IV (DSM IV-TR) criteria for substance dependence or Research Diagnostic Criteria for BED (Association, 2000). Subjects completed the UPPS-P Impulsive Behaviour Scale (Whiteside and Lynam, 2001) and Beck Depression Inventory (Beck et al., 1961). EtOH and obese subjects completed the Alcohol Use Disorders Identification Test (AUDIT) (Babor et al.) and obese subjects the Binge Eating Scale (BES) (Gormally et al., 1982). The National Adult Reading Test (Nelson, 1982) was used to obtain an index of premorbid IQ.

For the EtOH, Obese subjects with and without BED, primary diagnoses were confirmed by a psychiatrist using the Diagnostic and Statistical Manual of Mental Disorders, Version IV (DSM IV-TR) criteria for substance dependence or Research Diagnostic Criteria for BED (Association, 2000). Subjects >18 years old were included. HV, EtOH and obese subjects with and without BED, were excluded if they had a current major depression or other major psychiatric disorder including substance addiction (except nicotine), major medical illness or were on psychotropic medications. Etoh subjects were tested 2 weeks to 1 year after abstinence and >1 week after discontinuation of long-acting benzodiazepines used during detoxification. Subjects were excluded if they had a positive urine drug screens or alcohol breathalyzer test on testing day.

Meth subjects were tested one week to one year after abstinence and excluded if they had current major depressive episode of moderate severity (Beck Depression Inventory >20), other major psychiatric history or medical illness. Other forms of substance addiction were allowed assuming the primary drug for rehabilitation admission was methamphetamine (self-identified, highest frequency use and escalating use prior to admission). Regular drug screens were conducted at the rehabilitation centre. All psychiatric diagnoses in the Meth group were confirmed by a psychiatrist using DSM IV-TR criteria.

For HV, Etoh and obese subjects with and without BED, two separate specifically designed questionnaires were used to assess drug use (e.g. type, duration of use, amount per week, last use). Psychiatric disorders were screened using the Mini

International Neuropsychiatric Interview (Sheehan et al., 1998). Subjects completed the UPPS-P Impulsive Behaviour Scale (Whiteside and Lynam, 2001) and Beck Depression Inventory (Beck et al., 1961). EtOH and obese subjects completed the Alcohol Use Disorders Identification Test (AUDIT) (Babor et al.) and obese subjects the Binge Eating Scale (BES) (Gormally et al., 1982). The National Adult Reading Test (Nelson, 1982) was used to obtain an index of premorbid IQ. Subjects were paid for their study participation time and told they could receive an additional amount (£5) for their performance. Subjects in Minnesota were given the equivalent amount in a department store gift card. The study was approved by the University of Cambridge Research Ethics Committee and the University of Minnesota Institutional Review Board.

MRI Data Acquisition and analysis

Imaging data was acquired at the Wolfson Brain Imaging Centre at the University of Cambridge using a Siemens 3T Tim Trio 3T scanner (Siemens Medical System Systems, Erlangen, Germany). Anatomical images were obtained using a T1-weighted structural image using an MPRAGE sequence (TR=2300 ms; TE=2.98 ms; FOV 240 x 256 x 176 mm, voxel size 1x1x1 mm), with a 12 channel head coil. Statistical Parametric Mapping software (SPM8) (<http://www.fil.ion.ucl.ac.uk/spm>) was used for preprocessing. T1-weighted images were reoriented to the anterior commissure. We used New Segment which assigns a probability of each voxel belonging to a particular tissue class based on tissue probability maps. Grey matter images were used to generate a custom template using DARTEL (Ashburner, 2007). Template-space images were

transformed into ICBM152 MNI space using an affine transformation. Images were smoothed using an 8 mm FWHM isotropic Gaussian kernel. Grey matter volume was analyzed using a general linear model in a regression analysis with α as a dependent factor. Total intracranial volume using proportional scaling with an explicit mask using the brain mask template was used. All clusters greater than 5 voxels for FWE whole brain corrected $P < 0.05$ were considered significant.

Subject characteristics

Twenty-three Meth subjects (reported in mean (SD): weeks abstinent: 11.3 (20.04); years ever used: 10.16 (6.31); years of heavy use: 2.60 (2.51); Penn Craving Scale: 15.17 (9.17); mean use 0.5 gm/day reported in 16 subjects) (Table 1). In the Meth subjects, all subjects had completed high school and 18/23 had some college, graduate or post-graduate education. Data from 1 Meth subject were excluded due to a moderately severe current major depressive episode. Six Meth subjects had a concurrent alcohol use disorder and 21 used nicotine daily. Meth subjects had the following comorbid psychiatric diagnoses (lifetime major depression 4; panic disorder 1; post-traumatic stress disorder 1; obsessive compulsive disorder 1; anorexia nervosa/bulimia 1; compulsive sexual behaviors 2; attention deficit hyperactivity disorder 4). Meth subjects were on the following medications (antidepressants 9; mood stabilizer 3 (used also for pain); neuroleptic 2; medication status unknown 2). Thirty EtOH subjects (AUDIT 19.58 (SD 14.10); weeks abstinent 16.17 (SD 16.07); years of dependence 12.85 (SD 8.26); Units/day 27.86 (SD 14.18)) were recruited. EtOH subjects were on the following medications (acamprosate 2; disulfiram 1).

Results

Nicotine

HV subjects had included non-smokers (N=46), current smokers (N=17) and ex-smokers (N=11) and status unknown (N=12). Both Obese and BED subjects had the same proportion of smokers (N=4), ex-smokers (N=7) and non-smokers (N=18). We assessed $w(p)$ using a mixed measures ANOVA for reward and loss separately in smokers versus non-smokers and ex-smokers versus non-smokers focusing on the main Group effect controlled for age and gender. In the HV, there was a trend towards a Group effect in which smokers made more risky choices in the reward condition than non-smokers (Reward: $F(1,56)=3.514$; $p=0.066$); Loss: $F(1,56)=2.763$; $p=0.102$) but not in ex-smokers versus non-smokers (Reward: $F(1,56)=0.005$, $p=0.946$; Loss: $F(1,56)=1.502$, $p=0.226$). We combined the Obese and BED group and show that ex-smokers made fewer risky choices in the reward condition than non-smokers (Reward: $F(1,48)=4.586$, $p=0.037$; Loss: $F(1,48)=0.383$, $p=0.539$) but not current smokers versus non-smokers (Reward: $F(1,44)=1.087$, $p=0.365$; Loss: $F(1,44)=0.080$, $p=0.779$). To further assess the role of smoking on reward anticipation, we combined the Obese, BED and HV groups and show that ex-smokers (N=25) made fewer risky choices than non-smokers (N=82) ($F(1,103)=4.276$, $p=0.041$) but there were no differences between current smokers (N=24) and non-smokers (N=82) ($F(1,102)=1.471$, $p=0.228$). In the Meth group, there were no differences between smokers (N=14) and non-smokers (N=8) (Reward: $F(1,18)=0.006$, $p=0.940$; Loss: $F(1,18)=0.249$, $p=0.624$). In the EtOH group, there were no differences between current smokers (N=14) and non-smokers (N=12) (Reward: $F(1,22)=0.003$,

$p=0.954$); Loss: $F(1,22)=0.191$, $p=0.667$). Ex-smokers ($N=5$) were not assessed as the sample size was too small

Figure S1

A. Non-linearity of probability weighting (Kahneman and Tversky, 2000). The value of the outcome value is weighted by a decision weight, $w(p)$ (the subjective belief of the objective probability p). Lower probabilities are over-weighted leading to risk seeking for gains and risk aversion for losses. Higher probabilities are under-weighted leading to risk aversion for gains and risk seeking for losses.

B. Subjective value has a concave function reflecting diminishing subjective discrimination (marginal sensitivity) at higher values. The same increment at higher values (£1000 and £1010) has less subjective value than the same increment at lower values (£10 and £20).

Figure S2.

Risk task. Example of staircase procedure used to determine certainty equivalent (CE). The value (V) of the Risky choice (amount indicated over the jar) was calculated as $V=EV/P$ (e.g. for $P=0.1$, $EV=£100$, $V=£1000$). The CE range was

determined by defining values between the range of 0 and V of the Risky choice (e.g. 0 to £1000). In trials 1 and 2, the amount of the Sure choice was the one-third (e.g. £333) and two-third (e.g. £666) cut point values. In this example, the subject rejected the lower and middle third. The upper third was then used as the value range for which the one-third (e.g. £777) and two-third (e.g. £888) cut point values were used for the Sure choice for trials 3 and 4. The same process was repeated for trials 5 and 6. In this example, the subject rejected the middle and upper third. The lower third was then used as the value range for which the one-third (e.g. £703) and two-third (e.g. £740) cut point values were used for the Sure choice trials for trials 5 and 6. The average of these final choices was used to determine the CE.

Table S1. Subject characteristics and behavioural measures

	EtOH	HV - EtOH	T P	Meth	HV - Meth	T P
N	30	60		22	44	
Age	41.40 (11.57)	42.53 (11.41)	0.441 0.660	31.05 (4.78)	32.35 (6.41)	0.982 0.329
Males (N)	18	36		21	37	
IQ	114.32 (6.76)	115.54 (5.91)	0.880 0.382	108.89 (4.59)	111.95 (5.14)	2.360 0.021
BDI	12.89 (9.29)	5.35 (5.91)		15.32 (8.13)	4.97 (6.13)	5.786 <0.001
UPPS	154.25 (20.14)	121.35 (25.39)	4.682 <0.001	156.71 (22.47)	122.39 (20.29)	6.250 <0.001
AUDIT	19.59 (14.10)	5.01 (3.99)	7.470 <0.001			

Table S1. Subject characteristics and behavioural measures

Abbreviations: EtOH = abstinent alcohol dependent subjects; HV = healthy volunteers; Meth = abstinent methamphetamine dependent subjects; N = number of subjects; BDI = Beck Depression Inventory; UPPS = UPPS Impulsive Behaviour Scale; AUDIT = Alcohol Use Disorders Identification Test

Table S2. Subject characteristics and behavioural measures in obesity.

	Obese	HV	T	Obese	HV	T

	BED		P	control		P
N	30	60		30	60	
Age	42.92 (8.59)	43.95 (10.91)	0.451 0.653	44.06 (9.70)	42.91 (9.98)	0.520 0.604
Males (N)	13	26		19	38	
IQ	115.95 (6.67)	114.83 (6.98)	0.728 0.469	115.18 (6.45)	114.89 (6.71)	0.196 0.845
BDI	12.50 (6.52)	5.91 (5.68)	4.937 <0.001	6.96 (5.92)	5.01 (5.94)	1.470 0.145
UPPS	132.60 (19.98)	122.31 (22.81)	2.100 0.039	128.95 (19.89)	122.85 (23.92)	1.203 0.2321
BMI	34.68 (5.49)	22.95 (2.68)	13.660 <0.001	32.72 (3.41)	23.84 (2.91)	2.878 <0.001
BES	24.70 (7.56)	6.98 (6.95)	11.063 <0.001	8.67 (7.08)	7.15 (7.68)	0.908 0.366
AUDIT	6.11 (5.51)	5.62 (3.91)	0.487 0.628	4.09 (3.99)	4.93 (4.01)	0.938 0.351

Table S2. Subject characteristics and behavioural measures in obesity.

Abbreviations: BED = Obese subjects with binge eating disorder; HV = healthy volunteers; Obese control = Obese subjects without binge eating disorder; N = number of subjects; BDI = Beck Depression Inventory; UPPS = UPPS Impulsive Behaviour Scale; BMI = body mass index; BES = binge eating scale; AUDIT = Alcohol Use Disorders Identification Test

Table S3. Mixed measures ANOVA: Group, Valence, Probability and Value

	BED	Obese	Etoh	Meth
Group	(1,86)=4.831 0.030	(1,87)=2.312 0.132	(1,86)=5.031 0.027	(1,62)=14.993 <0.001
Prob	(3,84)=83.261 <0.001	(3,85)=81.676 <0.001	(3,84)=87.114 <0.001	(3,60)=68.784 <0.001
Valence	(1,86)=0.077 0.782	(1,87)=10.924 0.001	(1, 86)=2.231 0.139	(1,62)=0.622 0.433
Value	(3,84)=10.184 <0.001	(3,85)=13.802 <0.001	(3,84)=3.006 0.035	(3,60)=4.234 0.006
Group x Prob	(3,84)=4.982 0.002	(3,85)=5.288 0.001	(3,84)=6.237 0.001	(3,60)=14.485 <0.001
Group x Valence	(1,86)=5.144 0.026	(1,87)=0.251 0.62	(1,86)=1.394 0.241	(1,62)=1.248 0.268
Group x Value	(3,84)=2.120 0.098	(3,85)=0.729 0.54	(3,84)=5.146 0.002	(3,60)=4.296 0.006
Group x Valence x Prob	(3,84)=4.262 0.006	(3,85)=10.550 <0.001	(3,84)=4.248 0.007	(3,60)=4.118 0.009

Table S3. Mixed measures ANOVA: Group, Valence, Probability and Value

Abbreviations: BED = Obese subjects with binge eating disorder; Obese = Obese subjects without binge eating disorder; EtOH = abstinent alcohol dependent subjects; Meth = abstinent methamphetamine dependent subjects. Prob = probability

Table S4. Mixed measures ANOVA: Group, Probability and Value for Reward and Loss

	BED	Obese	Etoh	Meth
REWARD				
Group	(1,86)=10.873 0.001	(1,87)=0.483 0.489	(1,86)=5.301 0.024	(1,62)=12.955 0.001
Prob	(3,84)=62.198 <0.001	(3,85)=64.719 <0.001	(3,84)=64.376 <0.001	(3,60)=38.251 <0.001
Value	(3,84)=6.134 0.001	(3,85)=18.644 <0.001	(3,84)=11.034 <0.001	(3,60)=2.962 0.038
Group x Value	(3,84)=2.812 0.044	(3,85)=1.528 0.212	(3,84)=1.587 0.198	(3,60)=3.408 0.038
Group x Prob	(3,84)=1.126 0.344	(3,85)=0.448 0.719	(3,84)=0.793 0.501	(3,60)=6.442 0.001

Group x	(9,86)=0.722	(9,87)=2.458	(9,86)=1.555	(9,54)=0.743
Value x	0.688	0.015	0.142	0.668
Prob				
LOSS				
Group	(1,86)=0.354	(1,87)=1.753	(1,86)=0.224	(1,62)=4.320
	0.553	0.189	0.637	0.041
Prob	(3,84)=40.523	(3,85)=27.948	(3,84)=31.050	(3,60)=29.165
	<0.001	<0.001	<0.001	<0.001
Value	(3,84)=3.525	(3,85)=3.254	(3,84)=0.640	(3,60)=1.271
	0.018	0.025	0.591	0.291
Group x	(3,84)=1.359	(3,85)=0.383	(3,84)=2.670	(3,60)=1.234
Value	0.260	0.765	0.052	0.304
Group x	(3,84)=4.659	(3,85)=9.947	(3,84)=10.407	(3,60)=14.299
Prob	0.004	<0.001	<0.001	<0.001
Group x	(9,86)=1.056	(9,87)=0.860	(9,86)=1.671	(9,54)=2.300
Value x	0.403	0.564	0.109	0.026
Prob				

Table S4. Mixed measures ANOVA: Group, Probability and Value for Reward and Loss

Abbreviations: BED = Obese subjects with binge eating disorder; Obese = Obese subjects without binge eating disorder; EtOH = abstinent alcohol dependent subjects; Meth = abstinent methamphetamine dependent subjects. Prob = probability

Table S5. Convexity (β) and non-linearity (α) of probability weighting measures

		BED	Obese	Etoh	Meth
β	Group	(1,83)=17.98	(1,85)=0.46	(1,83)=5.29	(1,50)=6.82
		<0.001	0.501	0.024	0.012
	Prob	(3,81)=6.93	(3,83)=13.02	(3,81)=11.28	(3,48)=1.33
		<0.001	<0.001	<0.001	0.276
α	Group	(3,81)=2.55	(3,83)=1.55	(3,81)=1.38	(3,48)=3.79
	x	0.060	0.209	0.255	0.016
	Prob				
α	Group	(1,83)=0.23	(1,85)=0.12	(1,83)=0.44	(1,50)=8.53
		0.64	0.729	0.51	0.004
	Prob	(3,81)=4.59	(3,83)=2.82	(3,81)=2.64	(3,48)=3.73
		0.005	0.044	0.060	0.011
α	Group	(3,81)=0.52	(3,83)=1.45	(3,81)=2.35	(3,48)=1.23
	x	0.67	0.235	0.082	0.32
	Prob				

Table S5. Convexity (β) and non-linearity (α) of probability weighting measures

Abbreviations: BED = Obese subjects with binge eating disorder; Obese = Obese subjects without binge eating disorder; EtOH = abstinent alcohol dependent

subjects; Meth = abstinent methamphetamine dependent subjects. Prob = probability

- Ashburner J (2007) A fast diffeomorphic image registration algorithm. *NeuroImage* 38:95-113.
- Association AP (2000) Diagnostic and statistical manual of mental disorders (4th Ed., text rev). Washington, D.C.: American Psychiatric Association.
- Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG The Alcohol Use Disorders Identification Test, Guidelines for Use in Primary Care, Second Edition. In: Department of Mental Health and Substance Dependence, World Health Organization.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J (1961) An inventory for measuring depression. *Archives of general psychiatry* 4:561-571.
- Gormally J, Black S, Daston S, Rardin D (1982) The assessment of binge eating severity among obese persons. *Addictive behaviors* 7:47-55.
- Nelson HE (1982) National Adult Reading Test. In. Windsor, UK: NFER-Nelson.
- Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC (1998) The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 59 Suppl 20:22-33;quiz 34-57.
- Whiteside SP, Lynam DR (2001) The five factor model and impulsivity: using a structural model of personality to understand impulsivity. *Personality and Individual Differences* 30:669-689.