Figure legends

Figure 1 Excessive alcohol-drinking model

Rats and mice experienced 7-8 weeks of intermittent access to 20% alcohol two-bottle choice drinking paradigm (IA20%-2BC). Control animals had access to water (W) only. Brain regions were removed after a short period of access to alcohol (Binge, 30 min after the last drinking session in rats, 4 hrs in mice) or after a withdrawal period of 24 hrs after the end of the last drinking session (Withdrawal).

Figure 2 Excessive alcohol intake activates AKT/mTORC1 signaling in the rat nucleus accumbens shell

After 7-8 weeks of IA20%-2BC, the core and shell subregions of rats NAc were removed 30 min after the beginning of the last drinking session (Binge, B, see Fig.1). (a,b) Phosphorylation of AKT and S6 was determined by western blot analysis. ImageJ was used for optical density quantification. Data are expressed as the average ratio +/- S.E.M of phospho-AKT to AKT and phospho-S6 to S6 and are expressed as percentage of water (W) control. Significance was determined using two-tailed unpaired *t*-test. (a) Phosphorylation level of AKT and S6 in the NAc core of binge drinking rats (B) pAKT ***p*>0.05**; pS6 ***p*>0.05**. n= 7 per group. (b) Phosphorylation level of AKT and S6 in the NAc shell of binge drinking rats (B) pAKT ***p*<0.001**; pS6 ***p*<0.05**. n=7 per group. (c) IHC analysis of phospho-S6 levels in the NAc shell and core of binge-drinking rats (B) compared to water (W) controls. Representative images of rat NAc labeled with phospho-S6 in red and NeuN in green. Bar scale 5x, 500µm; 20x, 80µm. Phospho-S6 labeled cells are expressed as percentage of water controls. Phospho-S6 in NAc core **p>0.05**; phospho-S6 in NAc shell ***p*<0.001**. n=7 per group. *p<0.05; ***p<0.001.

Figure 3 AKT/mTORC1 activation by alcohol in nucleus accumbens shell is long lasting and specific

(a) After 7-8 weeks of IA20%-2BC, the NAc shell of rats was removed after 24 hrs of withdrawal following the end of the last drinking session (Withdrawal, WD, see Fig.1), and the phosphorylation of AKT and S6 in the NAc shell was determined by western blot analysis. ImageJ was used for optical density quantification. Data are expressed as the average ratio +/- S.E.M of phospho-AKT to AKT and phospho-S6 to S6 and are expressed as percentage of water (W) controls. Significance was determined using two-tailed unpaired *t*-test. pAKT ***p*<0.01**; pS6 ***p*<0.05**. n=6 for alcohol group, n=7 for water group. (b) A diagram depicting the 10% continuous access 2 bottle choice (CA10%-2BC) alcohol drinking paradigm. Rats experienced 3 weeks (21 sessions) of CA10%-2BC. Controls animals had access to water (W) only. Brain regions were removed at the end of the last drinking session. Phosphorylation of AKT and S6 in the NAc shell after CA10%-2BC (CA) was determined by western blot analysis. pAKT ***p*>0.05**; pS6 ***p*>0.05** n=4 per group. (c) Intermittent access to a natural reward. Rats experienced 7-8 weeks of IA to 1% sucrose in the two-bottle choice drinking paradigm (IA1%-2BC). Control animals had access to water (W) only. Brain regions were removed 30 min after the beginning of the last drinking session. Phosphorylation of AKT and S6 in the NAc shell after IA1%-2BC (Suc) was determined by western blot analysis. pAKT ***p*>0.05**; pS6 ***p*>0.05** n=5 for sucrose group, n=4 for water group. *p<0.05; **p<0.01.

Figure 4 Excessive alcohol intake does not activate AKT/mTORC1 signaling in the rat dorsal striatum

After 7-8 weeks of IA20%-2BC, the DMS and DLS of rats were removed 30min after the beginning of the last drinking session (Binge, B, see Fig.1). (a,b) Phosphorylation of AKT and S6 was determined by western blot analysis. ImageJ was used for optical density quantification. Data are expressed as the average ratio +/- S.E.M of phospho-AKT to AKT and phospho-S6 to S6 and are expressed as percentage of water (W) controls. Significance was determined using two-tailed unpaired *t*-test. (a) Phosphorylation level of AKT and S6 in the DMS of binge drinking rats (B) pAKT ***p*>0.05**; pS6 ***p*>0.05**. n=7 per group (b) Phosphorylation level of AKT and S6 in the DLS of binge drinking rats (B) pAKT ***p*>0.05**; pS6 ***p*>0.05**. n=7 per group. (c) IHC analysis of phospho-S6 levels in the DMS and DLS of alcohol binge-drinking rats (B) compared to water (W) controls. Representative images of rat dorsal striatum labeled with phospho-S6 in red and NeuN in green. Bar scale 5x, 500µm; 20x, 80µm. Phospho-S6 labeled cells are expressed as percentage of the controls. Phospho-S6 in DMS ***p*>0.05**; phospho-S6 in DLS ***p*>0.05**. n=5 per group for DMS, n=7 per group for DLS.

Figure 5 Excessive alcohol intake activates AKT in the mouse dorsomedial but not in the lateral striatum and mTORC1 signaling is not activated in either striatal regions

After 7-8 weeks of IA20%-2BC, the DMS and DLS of mice were removed 4 hrs after the beginning of the last drinking session (Binge, B, see Fig.1). Phosphorylation of AKT and S6 was determined by western blot analysis. ImageJ was used for optical density quantification. Data are expressed as the average ratio +/-S.E.M of phospho-AKT to AKT and phospho-S6 to S6 and are expressed as percentage of water (W) controls. Significance was determined using two-tailed unpaired *t*-test. (a) Phosphorylation level of AKT and S6 in the DMS of alcohol binge drinking mice (B) pAKT ***p*<0.01**; pS6 ***p*>0.05**. n=11 per group. (b) Phosphorylation level of AKT and S6

in the DLS of binge drinking mice (B) pAKT ***p*>0.05**; pS6 ***p*>0.05**. n=11 per group. (c) Phosphorylation level of AKT and S6 in the DMS of mice after a 24-hr period of withdrawal (WD) pAKT ***p*>0.05**; pS6 ***p*>0.05**. n=4 per group.**p<0.01

Figure 6 Excessive alcohol intake does not activate AKT/mTORC1 signaling in the rat medial prefrontal cortex

(a,b) After 7-8 weeks of IA20%-2BC, the mPFC of rats was removed 30min after the beginning of the last drinking session (Binge, B, see Fig.1). (a) Phosphorylation of AKT and S6 was determined by western blot analysis. ImageJ was used for optical density quantification. Data are expressed as the average ratio+/- S.E.M of phospho-AKT to AKT and phospho-S6 to S6 and are expressed as percentage of water (W) controls. Significance was determined using two-tailed unpaired *t*-test. Phosphorylation level of AKT and S6 in the mPFC of alcohol binge drinking rats (B) pAKT ***p*>0.05**; pS6 ***p*>0.05**. n= 7 per group (b) IHC analysis of phospho-S6 levels in the mPFC of alcohol binge-drinking rats (B) compared to water (W) controls. Representative images of rat mPFC labeled with phospho-S6 in red and NeuN in green. Bar scale 5x, 500µm; 20x, 80µm. Phospho-S6 labeled cells are expressed as percentage of the control. Phospho-S6 in mPFC ***p*>0.05**. n=7 per group. (c) After 7-8 weeks of IA20%-2BC, the mPFC of mice was removed 4 hrs after the beginning of the last drinking session (Binge, B, see Fig.1). Phosphorylation level of AKT and S6 in the mPFC of alcohol binge drinking mice (B) pAKT ***p*>0.05**; pS6 ***p*>0.05**. n=12 for alcohol group, n=10 for water group.

Figure 7 Excessive alcohol intake activates AKT/mTORC1 signaling in the rat orbitofrontal cortex

After 7-8 weeks IA20%-2BC, the OFC of rats were removed 30 min after the beginning of the last drinking session (Binge, B, see Fig.1) **(a,b)** or 24 hrs after the end of the last drinking session (Withdrawal, WD) **(c)**. Phosphorylation of AKT and S6 was determined by western blot analysis. ImageJ was used for optical density quantification. Data are expressed as the average ratio +/- S.E.M of phospho-AKT to AKT and phospho-S6 to S6 and are expressed as percentage of water (W) controls. Significance was determined using two-tailed unpaired *t*-test. (a) Phosphorylation level of AKT and S6 in the OFC of alcohol binge drinking rats (B) pAKT ***p*<0.001**; pS6 ***p*<0.05**. n=7 per group **(b) IHC analysis of phospho-S6 levels in the OFC of alcohol binge-drinking rats (B) compared to water (W) controls. Representative images of rat OFC labeled with phospho-S6 in red and NeuN in green. Bar scale 5x, 500µm; 20x, 80µm. Phospho-S6 labeled cells are expressed as percentage of the control. Phospho-S6 in OFC *p*<0.001. n=7 per group. (c) Phosphorylation level of AKT and S6 in the OFC of rats after 24 hrs of withdrawal (WD) pAKT *p*<0.001; pS6 *p*<0.001. n=7 per group. *p<0.05; ***p<0.001.**

Figure 8 Excessive alcohol intake activates AKT/mTORC1 signaling in the mouse orbitofrontal cortex

After 7-8 weeks of IA20%-2BC, the OFC of mice were removed 4 hrs after the beginning of the last drinking session (Binge, B, see Fig.1) (a) or 24 hrs after the end of the last drinking session (Withdrawal, WD) (b). Phosphorylation of AKT and S6 was determined by western blot analysis. ImageJ was used for optical density quantification. Data are expressed as the average ratio +/- S.E.M of phospho-AKT to AKT and phospho-S6 to S6 and are expressed as percentage of water (W) controls. Significance was determined using two-tailed unpaired *t*-test. (a)

Phosphorylation level of AKT and S6 in the OFC of alcohol binge drinking mice (B) pAKT ***p*<0.001**; pS6 ***p*<0.001** n=10 per group. (b) Phosphorylation level of AKT and S6 in the OFC of mice after 24 hrs of withdrawal (WD) pAKT ***p*>0.05**; pS6 ***p*>0.05**. n=8 per group.***p<0.001.

Figure 9 Moderate consumption of alcohol as well as sucrose consumption do not activate AKT/mTORC1 signaling in the orbitofrontal cortex

(a) Phosphorylation of AKT and S6 in the OFC of rats after 3 weeks of CA10%-2BC was determined by western blot analysis. Phosphorylation of AKT and S6 was determined by western blot analysis. ImageJ was used for optical density quantification. Data are expressed as the average ratio +/- S.E.M of phospho-AKT to AKT and phospho-S6 to S6 and are expressed as percentage of water (W) controls. Significance was determined using two-tailed unpaired *t*-test. pAKT ***p*>0.05**; pS6 ***p*>0.05**. n=4 per group. (b) Phosphorylation of AKT and S6 in the OFC after 7-8 weeks of IA1%-2BC of sucrose was determined by western blot analysis. pAKT ***p*>0.05**; pS6 ***p*>0.05**. n=5 for sucrose group, n=4 for water group.