Our results suggest that FLX treatment induces dematura-
tion of the FC and hippocampus of adult mice with respect to
genome-wide gene expression patterns. The dematuration of
these brain regions might be involved in the therapeutic mecha-
nism of FLX and/or some of its adverse effects.

**PS132**

**Title:** Possible additional antidepressant-like mecha-
nism of sodium butyrate: Targeting the hippocampus

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**Abstract**

Chromatin remodeling mediated by histone acetylation might
be involved in the pathophysiology and the treatment of depres-

ion. Recently, it has been reported that the histone deacetyl-
ase (HDAC) inhibitors, such as sodium butyrate (SB), could be
a potential therapeutic agent for depression treatment. In the
present study, we aimed to clarify the antidepressant mecha-
nism of SB in the hippocampus. The mice were exposed to
chronic restraint stress (CRS) for 14 consecutive days (2h/day)
to induce depression-like behaviors. To assess depression-like
behaviors, sucrose preference test, light dark test (LD), tail sus-
pension test (TST), and forced swim test (FST) were performed
after CRS. We observed that CRS decreased HDAC2 and 5 mRNA
and protein levels in the hippocampus. In addition, SB co-treat-
ment decreased the depression-like behaviors that are induced
by CRS. SB prevented and normalized the phosphorylation of
cAMP response element binding protein (pCREB), acetylation of
histone H3 (AceH3), HDAC2, and brain-derived neurotrophic fac-
tor (BDNF) expression level that were decreased by CRS in the
hippocampus. These results suggest that the decreased HDAC2
and 5 expressions in the hippocampus of CRS may be a type of
spontaneous coping response against CRS. However, it seems to
be unsuccessful to prevent depression induction since reduction
of pCREB, AceH3 and BDNF were accompanied by CRS in the hip-

pocampus. Moreover, the reduced AceH3 level may be associ-
ated with the decreased pCREB, which appears to lead to the
depressed BDNF.

**Key words:** Depression, Sodium butyrate, CREB, BDNF, Histone
acetylation, Hippocampus

**Reference**

1. Han, A., Sung, Y.-B., Chung, S.-Y. & Kwon, M.-S. Possible addi-
tional antidepressant-like mechanism of sodium butyrate: Targeting the hippocampus. Neuropharmacology 81, 292–302 (2014).

**PS133**

**The role of Toxoplasma gondii in depression and anxiety - gene-environment interactions in the FSL rat model**

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**Abstract**

Toxoplasma gondii (TOX) is a common parasite affecting approxi-
mately one-third of the human population. An increasing
number of studies are providing evidence that the disease is
associated with behavioural changes and psychiatric disease.
Using the Flinders Sensitive-Line (FSL) rat model, the objective of
the current study was to characterize TOX-induced behavioural
changes and whether the behavioural outcome is affected by
 genetic vulnerability.

Rats were infected p.o. with 20 TOX-cysts. Twelve weeks post-
infection, the animals were subjected to a behavioural test-bat-
tery including tests for depression (sucrose-preference test (SPT)
and forced-swim test (FST)) and anxiety (elevated plus-maze
(EPM) and light-dark box (LDB)).

In the LDB TOX-infected animals, independent of pheno-
type, spent less time in the light area (p<0.05). In the EPM a
strain effect was found, with FSL animals spending less time in
the open arms compared to their FRL controls (p=0.01). Furth-
more, a strain X treatment interaction was found; when treated
with TOX, FRL animals spent as little time in the open arms
as the FSL animals (p=0.01). In the SPT an interaction
between strain and treatment was also found; vehicle treated
FSL animals did not show anhedonia when compared to FRL
animals, whereas TOX treated FSL, but not FRL, animals
displayed a marked decrease in sucrose consumption (p=0.010).
A similar interaction is found in the FST where FSL, but not FRL,
animals displayed increased despair following TOX treatment
(p<0.05).

These data show that TOX can induce anxiety-like behaviour
in rats independent of phenotype. Furthermore, we find that
genetically vulnerable FSL animals display more severe depres-
sive-like symptoms following TOX infection. Such results are in
line with clinical studies showing a marked increase of toxo-
plasmosis in anxiety patients compared to healthy controls
and moreover suggest an interplay between gene and environment
leaving genetically vulnerable subjects susceptible to depres-
sion induced by chronic toxoplasmosis.

**PS134**

**A strategy for treating in deficits of social behaviors
induced by exposure to social defeat stress as juveniles**

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**Abstract**

**Objective:** The persistent deficits of social behaviors in mice
exposed to social defeat stress as juveniles are useful for study-
ing the pathogenesis of psychiatric disorders following the
adverse childhood experiences. In the present study, we inves-
tigated a strategy for treating in deficits of social behaviors
induced by exposure to social defeat stress as juveniles.

**Methods:** The juvenile male C57BL/6J mice were exposed to a
male aggressive ICR mouse during 1 or 10 consecutive days.
Mice were acutely administered desipramine (a noradrenaline
reuptake inhibitor), sertraline (a selective serotonin reuptake
inhibitor), aripiprazole (a dopamine receptor partial agonist),
and memantine [a non-competitive N-methyl-D-aspartate
(NMDA) receptor antagonist] on 1 day after the last exposure
to social defeat stress. Administration of desipramine, sertraline,
and aripiprazole were also continued once a day for 15 days.
We assessed social behaviors at 1 and 15 days after the last exp-
sure to the stress. Monoamine turnover and phosphorylation of
Laboratory of Pharmacological Neuroendocrinology, Institute of treating to attenuate the treatment-resistant deficits. Serotonergic and dopaminergic activators or glutamatergic inhibitors may be a strategy for juveniles induces the development of antidepressant-treatment-resistant deficits of social behaviors related to monoaminergic and/or glutamatergic dysfunction. Serotonergic and dopaminergic activators or glutamatergic inhibitors may be a strategy for treating to attenuate the treatment-resistant deficits.

PS135
Effects of the mineralocorticoid receptor antagonist spironolactone in a treatment-resistant model of depression in female rats
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Abstract
In recent studies we have shown that the tryptophan (TRP) depletion model of depression previously validated in male rats is paroxetine-resistant in females (Franklin et al. 2015). In this model, we found that secretion of the mineralocorticoid hormone aldosterone increased after 4 days of TRP depletion and surprisingly prior to corticosterone enhancement. The study aim was to investigate the effects of mineralocorticoid receptor (MR) blockade on depression-like behaviour induced by TRP depletion.

Female rats were fed a control (0.2% of TRP) or low TRP diet (0.04% of TRP) for 14 days. They were simultaneously treated with the MR antagonist spironolactone (1.2 mg/rat/day) or placebo via matrix-driven delivery pellets (Innovative Research of America, USA) for 14 days. Rats were tested in the Forced Swim Test (FST) on treatment day 14. Animals were sacrificed by decapitation on day 15.

Two-way ANOVA showed that TRP depletion resulted in an increased immobility time in the FST. Further analysis showed that TRP-depleted rats treated with spironolactone but with placebo spent a significantly shorter time immobile compared to controls. Rats exposed to TRP depletion exhibited significantly higher serum concentrations of aldosterone and corticosterone, which were slightly modified by spironolactone treatment. TRP depletion significantly enhanced serum interleukin-6 as well as gene expression of orexin A, a neuropeptide related to ghrelin, which has been shown to be altered in patients with treatment-resistant depression.

Findings show that treatment of rats with the MR antagonist spironolactone results in a mild improvement of TRP depletion-induced depression-like behaviour. Blockade of aldosterone action could represent a target for new antidepressant treatment.

This study was supported by grant of VEGA 2/0128/14, APVV-14-0840 and HEIF 5 Funding (at Oxford Brookes University, Oxford, UK). Franklin et al., Neuroendocrinology, 102(4):274–287, 2015.

PS136
Time-dependent alteration of reward-induced dopamine release in the nucleus accumbens of the neuropathic pain model rats.
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Abstract
Chronic pain is frequently comorbid with psychiatric disorders such as depression, suggesting the common neuroplastic changes in the central nervous system. It has been considered that chronic pain lowers the function of mesolimbic reward circuits and leads to depression-like states. Nucleus accumbens (NAC) is one of the key structures of the mesolimbic dopaminergic system, which is well known to play an important role in the reward circuits. Extracellular dopamine (DA) levels in the NAC elevate after the acquisition or prediction of rewards. In this study, we examined the reward-induced DA release in the NAC of neuropathic pain model rats. To prepare the neuropathic pain model, the spinal nerve was ligated (SNL model), and reward-induced DA release in the NAC was examined 2 and 4 weeks after SNL surgery. The animals were given with two types of rewards, 30% sucrose solution or pain relief by intrathecally injection of pregabaline (100 μg/10 μl PBS), and DA release was monitored using an in vivo microdialysis technique. Both rewards increased extracellular DA levels in the NAC 2 weeks after SNL surgery. In contrast, neither sucrose solution nor pain relief increased the DA release 4 weeks after SNL surgery. These results suggest that dysfunction of the mesolimbic reward circuits occurred 4 weeks, but not 2 weeks, after SNL surgery.

PS137
Evidence that Cannabidiol Induces Acute Antidepressant-Like Effects in Different Animal Models
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Abstract
Objectives: Cannabidiol (CBD), a non-psychotomimetic compound of Cannabis sativa, induced antidepressant-like effects in rodents tested in the forced swimming and olfactory bulbectomy models (Zanelati et al., 2010, Linge et al., Neuropharmacology, 2015). However, no study so far has investigated CBD effects in animal models with greater construct validity for depression, such as the learned helplessness and the Flinders Sensitive and Resistant Line (FSL/FRL). The present work aimed at investigating the acute effects of CBD in these models.

Methods and Results: Experiment 1. For the learned helplessness (LH) paradigm male Wistar rats were submitted to the pre-test (inescapable footshocks) and test (escapable shocks) sessions with a seven days interval. A single injection of CBD (10, 30 mg/Kg, ip), imipramine (15 mg/Kg, ip) or vehicle was given to rats either after pre-test or 1h before test. Another group received daily injections of imipramine (15 mg/Kg/day, ip), between the pre-test and test, as a positive control for the antidepressant effect.