

**S51.05**

Treatment-seeking gamblers and Parkinson's disease: Case reports

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Pathological gambling (PG) is a rare but well-established behavioural disorders of Parkinson's disease (PD) patients treated with dopamine agonist. We investigate the chronological relationship between PD and diagnosis of PG within treatment-seeking gamblers.

**Sample and Methods:** From 174 consecutively admitted pathological gamblers we identified 4 patients with PD. Standardized medical records include socio-demographic characteristics, past gaming behaviours and gambling-treatment modalities as well as the evolution of PD and the pro-dopaminergic medication history.

**Results:** All four patients developed PG after the onset of PD treatment. Three patients described a period of chronic exposure to gaming facilities years before and after onset of pro-dopaminergic treatment, with occasional or regular gambling, but without a compulsive component. In one patient, PG appeared suddenly without any previous gaming behaviour after the onset of medication. Despite a high treatment motivation, gambling specific cognitive therapy was unsuccessful. (c) Implication for the Field

The relationship between PD and PG appears to be complex: Confounders such as psychosocial factors or increase in accessibility of gambling opportunities may account for these findings. This case series confirm that pro-dopaminergic treatment can induce PG behaviour, but may be more likely in "at risk" groups. These patients pose specific treatment challenges.

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## Symposium: The role of 5-HT1AR in pathophysiology and treatment of schizophrenia

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**S48.01**

The postsynaptic 5-HT1A-receptor and its role for cognitive functions in mice

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Schizophrenia is often accompanied by cognitive dysfunctions. Post-mortem and in vivo studies have revealed increased cortical 5-HT1A-receptor density and it was assumed that 5-HT1A-receptor active drugs could enhance cognition. Moreover, partial 5-HT1A-receptor agonists positively affected verbal memory in schizophrenic patients. However, the role of the 5-HT1A-receptor for cognition has not been fully clarified.

Recently, we have introduced transgenic mice overexpressing the 5-HT1A-receptor postsynaptically in the cortex and hippocampus. Function of the surplus receptors was verified by receptor activation with the agonist 8-OH-DPAT.

In this study we further investigated the role of postsynaptic 5-HT1A-receptors for cognition. Therefore, our mice were tested in the inhibitory avoidance, Morris water maze, and hole-board habituation task. Moreover, the effects of low and high doses of 8-OH-DPAT were examined in the inhibitory avoidance task.

Our transgenic mice showed no overall cognitive deficit. As a tendency, inhibitory avoidance retention was impaired in transgenic mice compared to wild-type controls. Both genotypes showed similar spatial learning abilities in the Morris water maze and habituated to the hole-board in a comparable manner. Anterograde amnesia induced by 8-OH-DPAT was in transgenic mice already apparent in a third of the dose used for wild-type mice. Retrograde amnesia could not be triggered.

Since the transgenic mice show untreated a rather normal behaviour, we assume that they possess compensatory mechanisms. However, after activation of the postsynaptic 5-HT1A-receptors the differences between wild-type and transgenic mice became more clear. Hence, our findings suggest that the cortical and hippocampal 5-HT1A-receptors play rather a modulatory role in learning.

**S48.02**

Effect of Serotonin-1A receptor on behavioral changes in animal model of schizophrenia-like behavior

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Some antipsychotics act as partial agonists on serotonin-1A receptors (5-HT1AR) localized postsynaptically in cortex and hippocampus and presynaptically on the serotonergic cell bodies and dendrites in raphe nuclei.

Our study's aim was to investigate the effect of pre- and postsynaptic 5-HT1AR activation on MK-801 (0.1, 0.3 mg/kg)-induced sensorimotor gating deficits and hyperlocomotion in a rat model of schizophrenia-like behavior. To investigate the effect of presynaptic receptor activation we used a partial agonist (buspirone; 1,10 mg/kg) and a low dose of full agonist (8-OH-DPAT; 0.025 mg/kg). The effect on both pre- and postsynaptic receptors was investigated by a high dose of full agonist (8-OH-DPAT; 1 mg/kg).

We found that buspirone in both doses had no effect on MK-801-induced deficit in sensorimotor gating. Contrarily, the low dose of 8-OH-DPAT ameliorated the deficit. The MK-801-induced hyperlocomotion was decreased by buspirone as well as by the low dose of 8-OH-DPAT. Activation of both pre- and postsynaptic 5-HT1AR had an opposite effect on MK-801-induced behavior.

Our findings accord with the published results that partial 5-HT1AR agonists could be effective in schizophrenia treatment, but full potent agonists could exacerbate psychotic symptoms. Observed differences between buspirone and the low dose of 8-OH-DPAT could be due to inhibition of D2 receptor.

This research was supported by grant MZ0PCP2005 from the MZCR and by the projects 1M0517 from the MSMT

**S48.03**

The influence of polymorphism for Serotonin 5HT-1A receptor on phenotypic variables in schizophrenia

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Dysfunction of the serotonin system has been implicated in schizophrenia. 5-HT1A and 5-HT2A serotonin receptors are involved in

the action of antipsychotic drugs. A common functional polymorphism (rs6295) in the promoter region of the human 5-HT1A receptor gene has been reported. This polymorphism may be useful in identifying psychopathology and phenotypic characteristics associated with altered function of the human 5-HT1A receptor.

The aim of this study was to determine whether genetic variants for these receptor influence the functional morphological characteristics of brain in schizophrenia.

63 patients with schizophrenia were genotyped for the functional variant in the promoter region of 5-HT1A receptor (rs6295) and for polymorphisms for 5-HT2A (rs6313) and serotonin transporter-SERT (rs4795541). The subjects were investigated by 18fluoro-deoxyglucose (18FDG) positron emission tomography (PET) in the resting state, magnetic resonance imaging (MR) and functional magnetic resonance (fMR) with 2-back test activation paradigm. Voxel-based-morphometry (VBM) was used to detect the differences in the density of grey and white matter. The neuroimaging data were treated by the use Statistical Parametric Mapping (SPM5) with genetic variants as the factor.

The polymorphism in 5-HT1A receptor was associated with the functional morphometric characteristics in cortical regions in projection areas of serotonergic system.

Our findings identify an important genetic factor predicting functional and structural characteristics in schizophrenia. Future research would test the role of HT1A polymorphism in the interaction with 5HT2A and SERT on morphological characteristics within the context of antipsychotic effects.

This research was supported by grant NR9324 (IGA MZCR) and by the project 1M0517 (MSMT).

## S48.04

Serotonin-1A agonists as a cognitive enhancer in schizophrenia: Clinical evidence

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**Background and Aims:** Postmortem and PET studies indicate increased serotonin (5-HT)-5-HT1A receptor density in frontal and temporal cortices in schizophrenia, suggesting up-regulation secondary to diminished 5-HT1A-receptor stimulation. We previously conducted a series of pilot studies of the effects of the addition of tandospirone, a 5-HT1A partial agonist and azapirone derivative, to ongoing treatment with small to moderate doses of typical antipsychotic drugs, on cognitive function in patients with schizophrenia. The addition of tandospirone (30 mg/day), but not placebo, for 4 to 6 weeks was found to improve executive function and verbal learning and memory.

**Methods and Results:** We have conducted a randomly-assigned placebo-controlled double-blind study to investigate the ability of the addition of buspirone to enhance cognitive function in subjects with schizophrenia treated with atypical antipsychotic drugs (AAPDs). Buspirone, 30 mg/day, outperformed placebo in improving the performance on a measure of attention/speeded motor performance and index of general cognitive function. The distinct cognition-enhancing ability of buspirone suggests its usefulness for patients who have large deficits in attention in spite of treatment with AAPDs.

**Conclusions:** The findings from these clinical studies indicate 5-HT1A receptors are a promising target for the management of psychotic symptoms and cognitive disturbances of schizophrenia. This

concept has prompted the development of novel antipsychotic compounds with agonist actions at 5-HT1A receptors, e.g. F156063, SLV313, SSR181507, and bifeprunox. Evidence from basic studies with these drugs suggests an optimal balance of activity at 5-HT1A and dopamine-D2 receptors is required to gain cognitive benefits, which deserves further investigations.

## Free Communications

### FC02.01

New psychotherapeutic package for PTSD- patients without marked personality disorders

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Cognitive models suggest that PTSD becomes persistent when individuals process the trauma in a way that leads to a sense of threat, which arises as a consequence of excessively negative appraisals of the trauma and its sequelae, and of a disturbance of autobiographical memory characterised by poor elaboration and contextualization, strong associative memory and strong conceptual priming. Nevertheless, despite adequacy and pertinence of the cognitive model of PTSD, recent neurobiological evidence shows that emotions can be experienced without cortical interpretations of stimuli, and clinical evidence indicates that experiences can be stored as isolated affective fragments that function later to distort cognition. This suggests that cognitive therapies are based on a limited model of mental functions that sometimes must be supplemented by broader approach, combined with classical cognitive therapy. EMDR for instance may be a specific treatment for non-cognitive driven and primary emotions, derived from direct activation of the amygdala. The actual impact of CBT on PTSD may be considered a result of the well known efficacy of those treatments on comorbid personality disorders or unipolar depression, which are often associated with PTSD. However, the usually high failure rate in treating PTSD along the lines of CBT may be due to its inefficacy on primary emotions, not-linked to cognitive dysfunction. Therefore, a combination of treatments targeting primary emotional disorders as well as secondary affective disorders, linked to cognitive distortions, may enhance efficacy of therapeutic management in PTSD.

### FC02.02

PTSD Symptoms: Results of trauma or correlates of psychosocial characteristics?

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**Background and Aims:** Reports in recent literature regarding PTSD note that: 1) defining symptoms do not always accompany exposure to a potentially traumatic event and 2) symptoms are often observed in the absence of experience with traumatic events. The question arises: is manifesting PTSD symptoms principally a function of experiencing traumatic events or of unrelated psychosocial characteristics.

**Methods:** Data on three sets of variables [PTSD symptoms (Intrusive Experiences and Defensive Avoidance), potentially traumatic experiences (victim of assault, witness of assault, experiencing domestic violence, experiencing interpersonal loss, injured in an accident) and psychosocial characteristics (availability of adult confidant, sense of personal efficacy, emotional reactivity)] were collected by