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## 170 – HIPPOCAMPUS-ACCUMBENS INTERACTIONS: THE CRITICAL ROLE OF MPFC

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**Introduction:** The ventral subiculum (vSub) of the hippocampus is proposed to gate information flow within the nucleus accumbens (NAc), a limbic region positioned to integrate information from limbic and cortical regions, including the media prefrontal cortex (mPFC). Moreover, the mPFC as well as the hippocampus are proposed to play a central role in the pathophysiology of schizophrenia. Therefore the aim of the current study was to examine the response of NAc neurons to vSub activation, and how this is modulated by the mPFC.
**Methods:** In vivo extracellular single unit recordings from NAc neurons were performed in chloral hydrate anesthetized rats. The response of NAc neurons to single pulse vSub stimulation was examined. In addition, the role of the mPFC in regulating vSub drive of NAc neurons was tested.
**Results:** Tetrodotoxin inactivation of the mPFC attenuated the ability of the vSub to drive spike firing in the NAc. However, when long-term potentiation (LTP) was induced in the vSub-NAc pathway, the vSub was now capable of driving the NAc without the participation of the mPFC. Moreover, this interaction was dependent upon activation of dopaminergic D2-receptors in the NAc.
**Conclusions:** This work underlines the critical role of the mPFC in the ability of vSub to drive NAc neurons. One model of schizophrenia posits that vSub hyperactivity may underlie both the hyperdopaminergic state and disruption of information flow in this circuit in schizophrenia. Therefore, inactivation of the mPFC, as would occur with PFC leucotomy in schizophrenia, may prevent the abnormal vSub drive of the NAc.

## 171 – HEMODYNAMIC CORRELATES OF P50 SUPPRESSION AND NETWORK OSCILLATIONS IN SCHIZOPHRENIA

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**Introduction:** Behavioral and electrophysiological data indicate compromised stimulus suppression in schizophrenia. The physiological basis of this effect and its contributions to the etiology of the disease are poorly understood.
**Methods:** Based on a modified P50-suppression paradigm, neural and metabolic measures of adaptation were studied in 12 patients with schizophrenia and 12 control subjects.
**Results:** First, amplitudes of left- and right-hemispheric induced oscillations were recorded with whole-head magnetoencephalography (MEG) whereas functional magnetic resonance imaging (fMRI), second, assessed the hemodynamic changes in response to pairs of beeps with a short interval (500 ms) as compared with those with a long interval (1,500 ms). The suppression of alpha power (8 - 13 Hz) time-locked to the stimuli was negatively correlated with the suppression of evoked components and the hemodynamic measures. Remarkably, the suppression of alpha power was reduced in the patients prior to stimulus onset.
**Conclusions:** Conceivably, alpha oscillations play a central role in stimulus adaptation of neuronal networks and reflect an active mechanism for sensory suppression. The reduced stimulus suppression in schizophrenia seems to be in part due to impaired generation of alpha oscillations in the auditory cortex, resulting in higher metabolic demand as detected by fMRI. We suggest that the reduced generation of alpha rhythm in the auditory domain may reflect an impaired gating function and, thus, contribute to sensory and cognitive deficits in schizophrenia.
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## 172 – A SIMPLE AUDITORY EVENT-RELATED POTENTIAL IS LINKED TO CEREBRAL GREY MATTER PATHOLOGY IN SCHIZOPHRENIA

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**Introduction:** 'Mismatch negativity' (MMN) amplitude reduction is well established in schizophrenia. MMN is an auditory event-related response (ERP) derived by subtracting the ERP to a frequent standard stimulus from the ERP to an infrequent deviant stimulus. Here we investigated the relationship of MMN and cortical grey matter in schizophrenia.
**Methods:** MMN and structural magnetic resonance images (sMRI) were collected from 18 schizophrenia subjects and 18 pair-wise age- and gender-matched healthy control subjects. MMN peak amplitudes were determined within 100 to 300 msec post-stimulus intervals f or three types of deviant stimuli that differed from the standard in duration, frequency and intensity. For the structural analysis, models were extracted from the sMRI of all subjects followed by the identification and tracing of sulcal landmarks. Average models of the cerebral cortex were generated using cortical pattern matching; a technique that maintains the relationship with the individual's scan while allowing the accurate averaging of gyral structures across subjects. Correlation maps of cerebral grey matter by peak amplitudes for each MMN type were calculated and tested by permutation analysis.
**Results:** Grey matter reduction in cortical areas subserving auditory processing, motor organization and executive function correlated with reduced MMN amplitude in patients to frequency deviants only. No correlations were observed in healthy controls.
**Conclusions:** These results suggest that frequency MMN amplitude reduction in schizophrenia reflects progressive loss of grey matter volume whereas duration and intensity MMN amplitude reductions that are evident early in the illness may precede cell loss.
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