Arterial blood samples are collected during the scanning sessions and provide information on the ratio between intact 18F-FDOPA and the primary metabolite. The input functions used for this data analysis are image derived based on the largest cerebral vessels and metabolite corrected. Regions of interest (ROIs) are manually drawn around the cerebellum and semi automatically around the basal ganglia. In this preliminary work, DSC values are based on Ki parameters obtained from slopes on Patlak plots.

**Results:** DSC has been measured at baseline on 16 patients (mean age 22.6 years, 5 males) and 18 HC (mean age 21.7 years, 9 males), with no significant difference in age or gender between groups. At baseline patients had a PANSS total score of 74 (SD 9.6) and GAF total score of 35 (SD 5.2).

No significant difference in Ki at baseline was shown between patients and HC. Clinical follow-up data was available on 12 patients. They received a mean Aripiprazole-dose of 9.3 (SD 3.9). Paired t-test showed a significant effect of treatment with a follow up PANSS total of 55 (SD 11.9), p<0.001 and GAF total of 49 (SD 11.2, p=0.002).

Six patients were characterized as responders, and six as non-responders using the Nancy Andresen remission criteria. There were no baseline differences in PANSS or GAF scores between responders and non-responders. Nor did the dose of Aripiprazole differ between these groups. There was however significant difference in the GAF total score at follow up (p =0.001), as GAF was 59 (SD 9.3) for responders and 39 (SD 5.3) for non-responders. Mean Ki-values at baseline was 0.79 (SD 0.2) for non-responders, 0.88 (SD 0.2) for responders and 0.91 (SD 0.2) for HC. One way ANOVA showed no significant group difference.

**Discussion:** Although not significant, we found a slightly lower Ki-value at baseline for non-responders compared to baseline Ki-values for responders and HC in these preliminary analyses. This was unexpected, but should be taken with precaution, as the results represent work in progress. Inclusion of subjects and data-analyses is ongoing, and data analysis will be more extensive in spring 2018, especially regarding the methodology: The current image derived input function suffers from partial volume effects (PVE). To account for PVE and other factors the image data will be co-registered with T1-weighted MRI data and normalized to standard space in order to use a standard anatomical atlas to help define the ROIs. Finally, as mentioned earlier, arterial samples are collected and we plan to use arterial input functions to correct for the complicated kinetics of the tracer. To improve the Ki estimation we will use the metabolite corrected arterial plasma curve as input function and compare these results with the current method.

**S151. SUBMISSION WITHDRAWN**

**S152. CANNABIDIOL INDUCED MODULATION OF MEDIOTEMPORAL ACTIVITY DURING A VERBAL MEMORY TASK IN FIRST-EPILOGE PSYCHOSIS**

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**Background:** Global neurocognitive impairments are a central feature of psychosis. Deficits in verbal memory in particular are the most consistently reported of these impairments from the first-episode of psychosis (FEP). Neuroimaging studies in psychosis have largely identified reductions in neural activation during various memory and learning related tasks, particularly in the medial temporal lobe, compared to healthy controls. Tetrahydrocannabinol (THC) and cannabidiol (CBD), both components of the cannabis plant that act through the endocannabinoid (eCB) system in the brain, have been found to induce direct and opposite neural effects during similar tasks in healthy samples, when compared to each other. Additionally, CBD has been shown to have antipsychotic properties, and may suppress THC induced psychotic symptoms and their directly associated functional abnormalities in healthy individuals. Thus far, the effects of CBD on the neural substrates implicated in memory and learning, and those underlying psychotic symptoms in FEP cohorts is unknown.

**Methods:** 17 FEP patients were initially recruited to the study. A double-blind, randomized, placebo controlled, repeated measures, within subject cross over design, with at least a one-week washout period between scans was employed. Participants were given identical capsules of either CBD (600mg), or placebo (PLB), then scanned using a block design fMRI paradigm, while performing a verbal paired associate learning task. 13 participants completed scanning, and were included in the analysis of the data. An ROI mask of the hippocampus, striatum, and parahippocampal gyrus was used in the data analysis, and all results were thresholded for less than one false positive over the whole map.

**Results:** A CBD related decrease in activity was observed in the left hippocampus (p = 0.0024) and the right parahippocampal gyrus (p = 0.0024) during the recall condition, within the FEP group. No significant differences between PLB and CBD functional activity were observed during the encoding condition. No significant differences were observed between FEP participant performances on the CBD and PLB study days.

**Discussion:** These findings provide robust evidence of the modulatory effect of an acute dose of CBD on the neural substrates underlying learning and memory, supporting a role for the eCB system in the abnormalities observed in psychosis, and its potential as a target for treatment.

**S153. WHERE IS THE ABNORMAL BRAIN ACTIVITY IN FIRST EPISODE PSYCHOSIS?**

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**Background:** Recent review about functional magnetic resonance imaging (fMRI) in first episode psychosis (FEP) concluded that there is an abnormal connectivity involving the frontal temporal pathway similar to found in chronic schizophrenia (Mwansisya et al., 2017). Besides, thalamic circuits were also altered in chronic schizophrenia patients (Li et al., 2017). The present work gives a wider review of studies using functional magnetic resonance imaging techniques (fMRI) on first-episode psychotic patients, specifically focus on the main areas involved.

**Methods:** The review was made in accordance with the PRISMA guidelines (Moher et al., 2009). For each study, the following factors were extracted: anatomical location of the main finding and type of functional abnormality (hypo and hyperactivation). A total of 3 different databases (PubMed, Web of Knowledge, Psychnfo) were reviewed. Thirty-five of 643 (from 2000 to 31st October 2017) neuroimaging papers were analyzed.

**Results:** We found that the dorsolateral prefrontal cortex (DLPFC) showed 52% of activity abnormalities (55% was hypoactivation). Temporal lobe

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showed 51% of functional activity altered (61% was hypoactivity). The ventrolateral prefrontal cortex (VLPFC) presented 28% of aberrant fMRI (75% was hyperactivity). Thalamus presented altered activation activity with 20% (71% was hypoactivity). The Cingulate was also altered during activation with 20% of patients (85% was hypoactivity). Finally, functional alterations of the Amygdala were present in 14% of the selected patients (80% was hypoactivation).

Discussion: This larger review suggests that there are several possible areas apart from fronto temporal pathways (Mwansisiya et al., 2017), that have to be taken into account at the early course of psychosis, such as limbic system, thalamo-cortical networks and cingulate. These functional activation abnormalities seem to be different to the reported in the previous review. The different results seem to be clearly influenced by the kind of paradigm. Moreover, our finding is not in concordance with the suggestion that thalamic alterations became only prominent at the chronic phase of psychosis (Li et al., 2017).

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S154. THE ROLE OF DOPAMINE IN PROCESSING THE MEANINGFUL INFORMATION OF OBSERVATIONS, AND IMPLICATIONS FOR THE ABERRANT SALIENCE HYPOTHESIS OF SCHIZOPHRENIA

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Background: The aberrant salience hypothesis of schizophrenia proposes that symptoms such as paranoia arise when behavioural salience is attributed to neutral stimuli. Mesolimbic dopamine dysfunction is thought to be central to this mechanism; building on findings that activity in this pathway conveys a (signed) reward prediction error signal. Given that many psychotic symptoms are not explicitly related to reward learning, it is relevant that recent studies in rodents have demonstrated a role for midbrain dopamine neurons in value-neutral associative learning. Direct evidence for this role in humans, however, is lacking.

In this study we asked whether the mesolimbic dopamine circuit is involved in encoding the value-neutral meaningful information of observations, using a model-based functional magnetic resonance imaging (fMRI) task and dopamine positron emission tomography (PET). We define ‘meaningful information’ as the degree to which an observation results in a belief-update to an agent’s internal model of the environment (Kullback-Leibler divergence from prior to posterior beliefs; ‘Bayesian surprise’).

Methods: Participants were tasked to infer the current (hidden) state of the environment, using partially-informative observations at each trial, and then report their belief at the end of each trial. Participant beliefs were modelled using a Hidden Markov Model of the task and iterative application of Bayes’ rule, allowing us to quantify the Bayesian surprise (meaningful information content) associated with a trial observation. Crucially, our task de-correlated Bayesian surprise from both the pure sensory unexpectedness of an observation (unexpected but meaningless information) and its signed reward prediction error. 39 healthy participants (22M, mean age 26y) performed 180 task trials within an fMRI scanner. 36 participants also had a [11C(+)4-propyl-9-hydroxy-naphthoxazine (PHNO) PET scan to quantify dopamine-2/3 receptor (D2/3R) availability. 17 participants additionally had a second PET scan 3hrs post 0.5mg/kg oral dexamphetamine, to quantify striatal dopamine release capacity. Neuroimaging analyses were restricted to the bilateral substantia nigra/ventral tegmental area (SN/VTA) and ventral striatum (VS).

Results: Our computational model closely predicted participant behaviour (R2= .67), and there was a negative correlation between subclinical paranoia and the degree to which participant behaviour approximated normative Bayesian performance (rho = -.60, P=0.001). Neuronal activation encoding the meaningful information content of an observation (Bayesian surprise) was present in SN/VTA and VS (both P(peak)<0.05, SVC), whereas no such encoding was present for sensory unexpectedness or reward-prediction error. Crucially, activation encoding Bayesian surprise was inversely correlated with D2/3R availability in the SN/VTA (rho = -.43, P=0.009), consistent with a tonic inhibitory role for midbrain D2/3Rs. Moreover, activation encoding Bayesian surprise was inversely related to dopamine release capacity in the VS (rho = -.66, P=0.005), indicating that subjects with high dopamine release capacity showed blunted striatal activation in response to belief-changing information, as is also found in schizophrenia.

Discussion: We provide direct evidence in humans that a mesolimbic dopamine circuit is involved in encoding the meaningful information content of observations, distinct from its involvement in processing signed reward prediction error. These results implicate dopamine in a wider range of function than reward learning, including updating a predictive associative model of the world, and are therefore relevant for the aberrant salience hypothesis of schizophrenia.

S155. SENSORY ATTENUATION DURING AUDITORY PROCESSING IN PARTICIPANTS AT CLINICAL-HIGH RISK FOR PSYCHOSIS: EVIDENCE FROM MAGNETOENCEPHALOGRAPHY

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Background: The ability to predict the sensory feedback of self-generated stimuli against incoming sensory information is of importance to distinguish internal from external stimuli and is associated with sensory attenuation. Furthermore, it has been proposed that deficits in sensory attenuation could contribute to clinical symptoms of schizophrenia, including hallucinations and delusions, involving potential deficits in corollary discharge. The current study examined the hypothesis whether sensory attenuation is present in participants at clinical high-risk (CHR) for psychosis.

Methods: Sixty-four CHR-participants and 32 healthy controls were presented with auditory stimuli during two experimental conditions: 1) In a