

Schizophrenia



- Schizophrenia affects 250,000 UK citizens and 2.2 m US citizens
 - Equally frequent in men and women but has an earlier onset in men (late teens/early twenties than women (twenties/early thirties)
- Current therapies (e.g. risperidone, olanzapine, aripiprazole) have significant limitations
 - Many patients are treatment resistant particularly their cognitive symptoms
 - Problematical side-effects including motor complications and weight gain
- Need for a well-tolerated treatment that improves cognitive symptoms
 - Registration trials require large numbers of patients due to placebo effects
 - Schizophrenic patients are difficult to recruit and few are drug free
- Experimental medicine studies of healthy volunteers with high and low schizotypy offers an alternative approach

Schizophrenia and Schizotypy



- Schizophrenia lies at extreme of normally distributed trait of psychosis proneness manifested as personality trait called schizotypy in general population
 - Features of schizotypal personality
 - Unusual experiences resembling attenuated psychotic symptoms
 - Unusual beliefs resembling delusions and cognitive deficits
 - Symptoms more common in relatives of patients with schizophrenia and led to identification of Schizotypal Personality Disorder (SPD)
- Component symptoms of SPD detectable in general and clinical populations
 - Use questionnaires such as Schizotypal Personality Questionnaire (SPQ) based on DSM-III-R criteria for SPD or Oxford Liverpool Inventory of Feelings and Experiences (O-LIFE)
 - Scores on schizotypal trait questionnaires = level of “psychosis proneness” or schizotypy

A collaboration with Bill Deakin, Emma Barkus and Shon Lewis University of Manchester

Schizotypy Recruitment



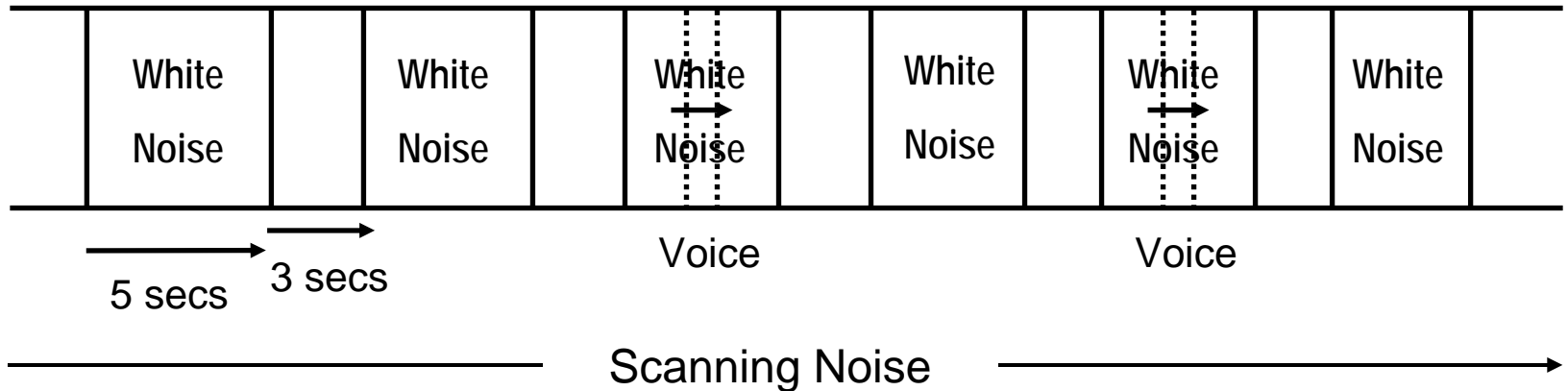
- In Manchester over 1000 students completed the O-LIFE using the intranet and more recently over 700 participants completed the SPQ within three months of being posted on the internet
 - In both cases schizotypy scores were normally distributed with mean approximating to published norms
 - High schizotypes from these non-clinical populations resemble patients with schizophrenia
 - Increased rates of non-localising (soft) neurological signs
 - Increased psychotic experiences after cannabis use
 - Cognitive biases
 - Participants selected on basis of extreme and mean schizotypy scores for follow up interviews and experimental medicine studies

Overall Hypothesis

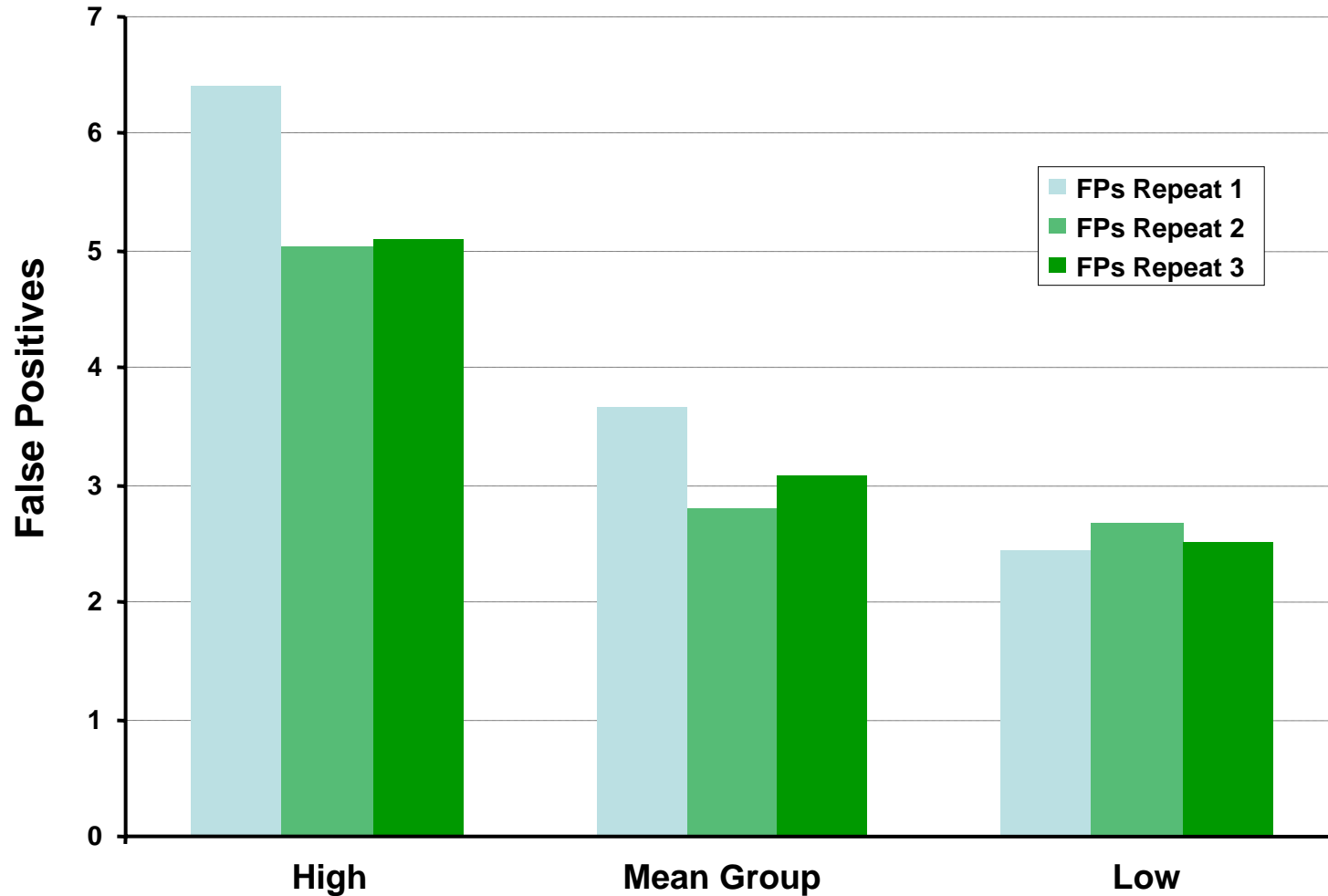


"That High scoring schizotypy can be identified in a non-clinical sample and distinguished from Mean and Low scoring schizotypes on the basis of performance in a signal detection task. Additionally, the High schizotypes will display similar areas of activation to patients with hallucinations when experiencing false positives in a fMRI scanner."

Signal Detection Experiment



Results – False Positives

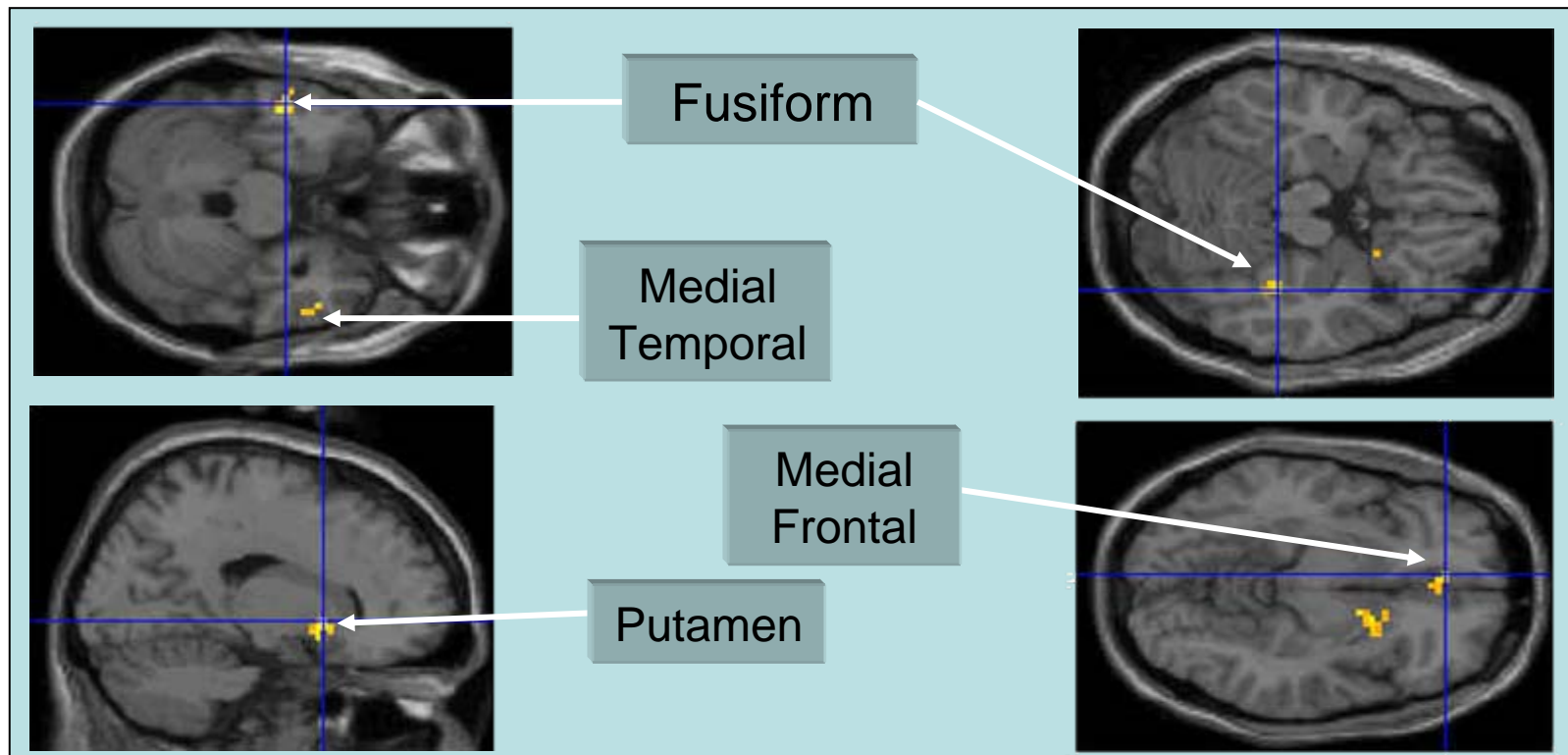


High group reported more FPs ($F=3.59, df=2, p=0.017$)

fMRI Preliminary Results



- Event related design
- Subtraction examining hallucinatory-like experiences = False Positives minus the Correct Rejections (True Negatives)



Conclusions and Next Steps



- Participants with high schizotypy scores had more false positives in a signal detection task and showed fMRI activation in brain regions associated with hallucinations in schizophrenic patients
- Do antipsychotics reduce false positives in signal detection paradigm
 - Is this especially marked in individuals who have high scores on schizotypy questionnaires
 - Is this especially marked in individuals who have genotypes associated with risk of psychosis e.g. COMT met allele
- Indirect fMRI to establish which areas mediate false positives (i.e. hallucinations) in individuals who have high scores on schizotypy questionnaires
 - Is fMRI BOLD signal modified by antipsychotics
- Potential to use behavioural and fMRI measures in participants with high schizotypy to predict efficacy of novel drugs for treating schizophrenia