Effects of High Schizotypy on Control of Eye Movements: Modulation by Antipsychotic Drugs and Nicotine

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Background: Oculomotor dysfunction has been well documented within schizophrenia spectrum populations and has been proposed to be a sensitive biomarker for antipsychotic and cognitive enhancing compounds. This study examined the effects of antipsychotics and nicotine on oculomotor performance and investigated whether individuals with subclinical levels of schizotypy-like symptoms (called high schizotypy) show a differential profile of drug response compared to controls.

Methods: In a randomized double blind, placebo-controlled study 233 participants were randomly assigned to one of 4 drug groups (nicotine, risperidone, amisulpride, placebo) and performed prosaccade (PS), antisaccade (AS) and smooth pursuit eye movements (SPEM) tasks. Participants were classified into high and average schizotypy groups measured by the Schizotypy Personal Questionnaire.

Results: Main effects of drug were found for PS gain, PS velocity and AS velocity (all p<0.01), indicating impaired performance with risperidone and amisulpride tended to disrupt saccade inhibition in controls but to improve it in high schizotypes. Both groups improved with nicotine treatment. For SPEM a trend for a main effect of drug was found for velocity gain (p=0.052), indicating reduced gain with risperidone irrespective of schizotypy level.

Discussion: In this study eye movement performance proved to be a sensitive measure of pharmacological treatment effects. The main findings were: (1) replication of previous findings of cognitive enhancing effects of nicotine on antisaccade performance; (2) risperidone caused a slowing of AS and PS peak saccade velocity a reduction in PS spatial accuracy and an impairment in the ability to match eye velocity to target velocity during SPEM; (3) for the key biomarker of antisaccade error rate, drug effects were modulated as predicted by schizotypy status - risperidone and amisulpride tend to disrupt saccade inhibition in controls but improve it in high schizotypes. Together these findings represent promising trends for future research investigating pharmacological and schizophrenia spectrum populations.

Here we combine the model of psychotic schizotypy with the biomarker approach to enhance our understanding of drug response characteristics in the schizophrenic spectrum.

Aims & Objectives

To examine the effects of antipsychotics and nicotine on oculomotor performance and to investigate whether individuals with subclinical levels of schizotypy-like symptoms (high schizotypy) show a differential profile of drug response compared to controls.

Materials & Methods

- 240 healthy volunteers were recruited as part of a multicentre study (Manchester, Cardiff, London).
- Recruitment:
  - Participants were asked to fill in an online version of Schizotypal Personality Questionnaire (SPQ), suitable participants repeated the SPQ under lab conditions and were divided into between (21-36 -control group; MSz) or high (≥21-36 -high schizotypy group (HSz)).
- Demographic data was collected and matched between the schizotypy groups (see Table 1).

Study design:

- Double-blind, randomised, placebo controlled, parallel study design with 9 study arms:
  - Placebo (PLA)
  - Risperidone-2mg (RIS)
  - Amisulpride-400mg (AMS)
  - Nicotine-7mg (NIC)

- Standard screening criteria and exclusions for pharmacological studies were applied on screening and randomization day.

Study tasks:

- Four possible peripheral positions of a black dot on white background (±7.2°, ±14.4°, ±21.6°) for the random duration of 1000-2000ms, 60 trials in total.

- Antisaccade task (AS): Prosaccade (PS): directional error rate, latency, amplitude gain, peak velocity.
- Smooth Pursuit task (SPEM): sinusoidal target velocities: 12°/s, 24°/s, 36°/s, 20 half-cycles: SPEM velocity gain, SPEM saccadic frequency.

- AS Task
  - Saccade Latency (ms)
  - Directional Error Rate (%)

- PS Task
  - Saccade Latency (ms)

- SPEM Task
  - Gain with males performing significantly better than females.
  - A main effect of task (F(2,183)=7.80, p<0.01) and gender (F(1,183)=4.31, p<0.05) was found for peak velocity with RIS impairing performance compared to PLA, AMS and NIC irrespective of schizotypy group (all p<0.01). See Figure 2 for details.

- No main effect of schizotypy group was observed in this study. A main effect of site was found for AS error rate (F(2,197)=8.79, p<0.01) indicating lower error rates in Cardiff compared to Manchester and London. A significant effect of gender (F(1,197)=4.31, p<0.05) was found for SPEM gains with males performing significantly better than females.

Discussion

- We were able to replicate previous findings of the cognition enhancing effects of NIC on antisaccade performance.
- RIS caused a slowing of peak saccade velocity and an impairment in the ability to match eye velocity to target velocity during SPEM.

- Antisaccade task sensitive to nicotine especially in high schizotypy.

Conclusions

- Multicentre cognitive biomarker studies are feasible and can be reliable.
- Further research investigating pharmacological influences on high risk and schizophrenia spectrum populations.

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References