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# EYE MOVEMENT RESEARCH IN ADULT PSYCHIATRY

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# Current Practice in Psychiatry

- Syndrome diagnosis based on interviews (phenomenology).
- Selection of treatment based on symptoms. Trial and error for different agents.
- Maintenance of treatment that produced symptom remission and has favorite adverse reaction profile.

# In search for biomarkers

- Objective diagnostic tools as opposed to phenomenology.
- Probes to understand the pathophysiology of psychiatric disorders.
- Endophenotypes to study genetics of psychiatric disorders.
- Tools in the decision of treatment alternatives and the efficacy of treatment.

# Why use eye movements?

- Much richer data set probing neural mechanisms
- Baseline conditions where patients perform as well (prosaccades)
- Information about many cognitive processes disturbed in these patients
- Easily recorded
- Easy tasks and instructions

**Rommelse et al 2008**

# Focus of this presentation

- Eye movement paradigms discussed will be smooth eye pursuit and saccades (prosaccades, antisaccades, memory saccades).
- Model psychiatric disorder will be schizophrenia with references on affective psychoses (bipolar disorder, major depression) and obsessive compulsive disorder.

# Objectives

- Sensitivity (dissociating patients from controls)
- Specificity (dissociating different psychiatric syndromes)
- Relation to psychopathology and medication status
- Heritability and influence of genetic factors
- Neural substrate of differences between patients and controls

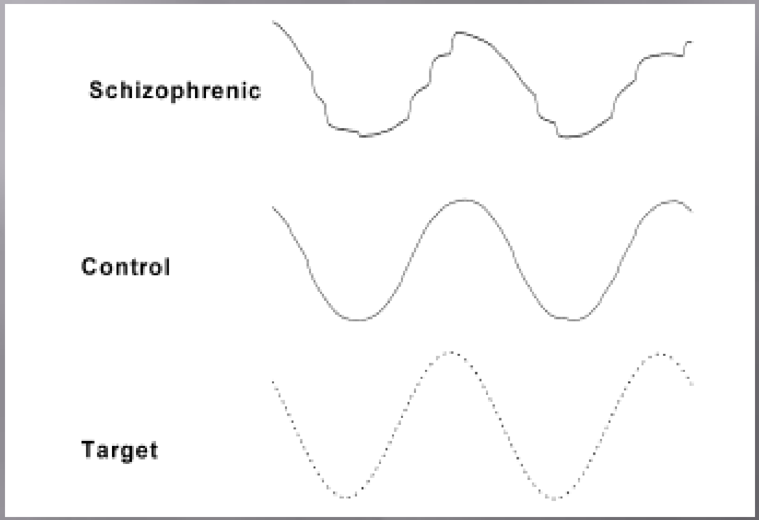
# History

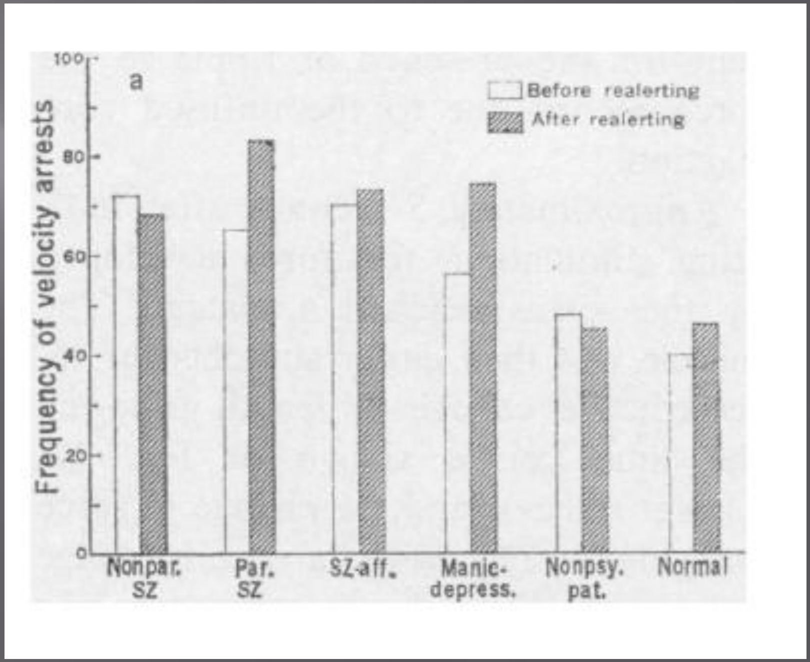
- In 1908 Diefendorf and Dodge using a method based on photography recorded eye movements during reading, visually guided saccades and smooth eye pursuit.
- "Insane" Patients (schizophrenia, bipolar disorder, depression etc) had worse smooth eye pursuit performance then controls.

# History

- In 1973 Holzman and colleagues used EOG to confirm worse pursuit in psychotic patients.
- In 1974 the same group showed deficits in smooth eye pursuit in first degree relatives of patients with schizophrenia.

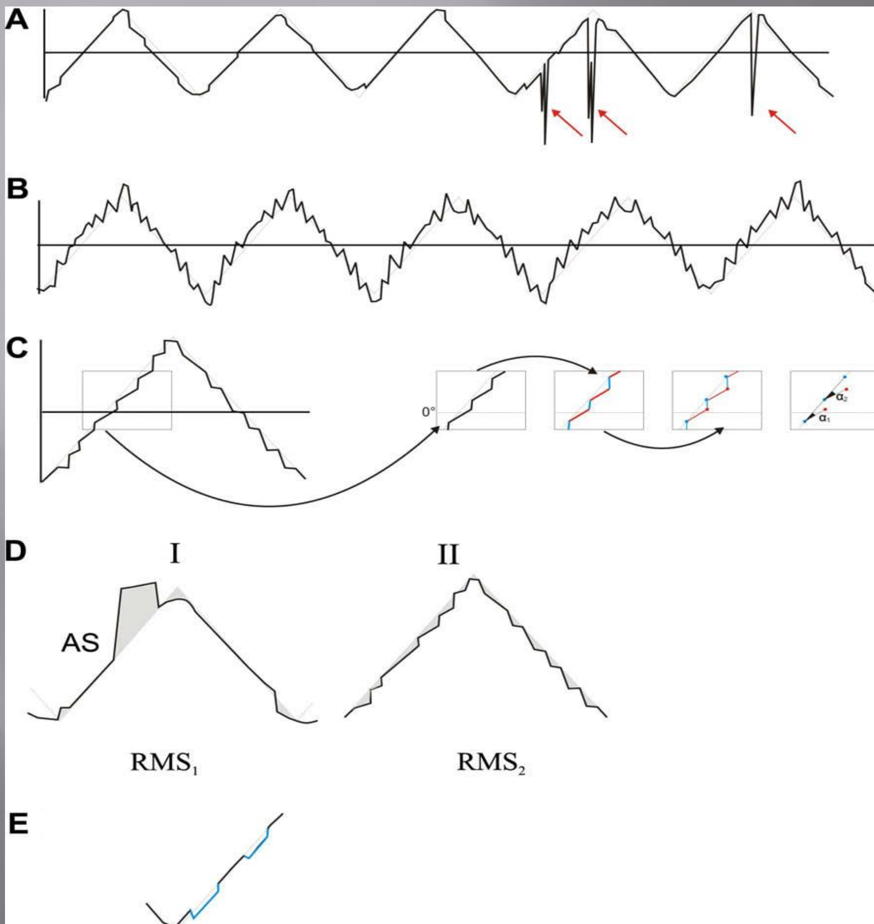
# Smooth pursuit abnormalities in schizophrenia



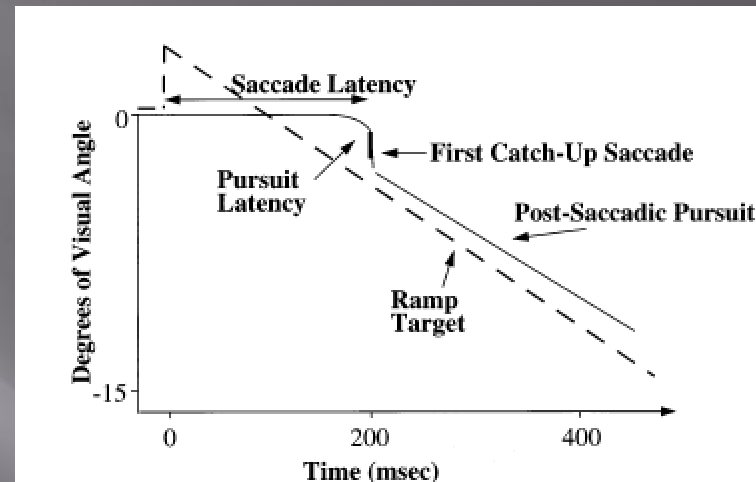




Holzman et al 1973

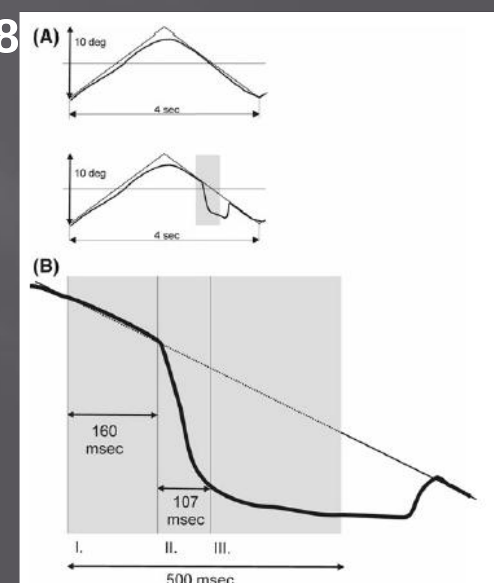
# Smooth Eye Pursuit performance measures




Smyrnis 2008




Sweeney et al 1998




Kattoulas et al 2011

# Test re-test reliability

**Table 1.** *Descriptive Statistics of Oculomotor Variables at Baseline and Retest (N = 21), Pearson and Intraclass Correlations (ICC), Repeatability Coefficients (RC), t Tests, and Effect Sizes (ES)*

| | Baseline | | Retest | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | *SD* | Mean | *SD* | Pearson | ICC | RC | *t* test | ES |
| SPEM gain 12°/s | 98.60 | 8.09 | 96.35 | 9.28 | $r = 0.11, p = .64$ | ICC = 0.10, $p > .10$ | 23.53 | $t = 0.92, df = 19, p = .37$ | 0.19 |
| SPEM gain 24°/s | 95.32 | 10.58 | 95.89 | 11.10 | $r = 0.31, p = .17$ | ICC = 0.31, $p > .10$ | 25.45 | $t = -0.21, df = 20, p = .84$ | −0.05 |
| SPEM gain 36°/s | 89.59 | 9.03 | 88.34 | 11.77 | $r = 0.81, p < .001$ | ICC = 0.77, $p < .01$ | 14.31 | $t = 0.84, df = 19, p = .41$ | 0.18 |
| SPEM gain 48°/s | 71.85 | 16.00 | 70.34 | 14.89 | $r = 0.71, p < .001$ | ICC = 0.70, $p < .01$ | 23.71 | $t = 0.58, df = 20, p = .57$ | 0.13 |
| AS 12°/s | 0.15 | 0.21 | 0.15 | 0.19 | $r = 0.94, p < .001$ | ICC = 0.93, $p < .01$ | 0.15 | $t = 0.53, df = 19, p = .60$ | 0.02 |
| AS 24°/s | 0.40 | 0.30 | 0.44 | 0.41 | $r = 0.59, p = .005$ | ICC = 0.56, $p < .01$ | 0.68 | $t = -0.51, df = 20, p = .62$ | −0.12 |
| AS 36°/s | 0.63 | 0.36 | 0.50 | 0.32 | $r = 0.79, p < .001$ | ICC = 0.73, $p < .01$ | 0.45 | $t = 2.25, df = 19, p = .04$ | 0.57 |
| AS 48°/s | 0.50 | 0.35 | 0.44 | 0.37 | $r = 0.59, p = .004$ | ICC = 0.58, $p < .01$ | 0.65 | $t = 0.89, df = 20, p = .38$ | 0.18 |
| CUS 12°/s | 0.29 | 0.09 | 0.26 | 0.14 | $r = 0.42, p = .07$ | ICC = 0.34, $p > .10$ | 0.22 | $t = 1.82, df = 19, p = .08$ | 0.27 |
| CUS 24°/s | 1.01 | 0.39 | 0.96 | 0.27 | $r = 0.64, p = .002$ | ICC = 0.59, $p < .01$ | 0.61 | $t = 0.70, df = 20, p = .49$ | 0.17 |
| CUS 36°/s | 1.84 | 0.66 | 1.69 | 0.70 | $r = 0.60, p = .005$ | ICC = 0.58, $p < .01$ | 1.23 | $t = 0.96, df = 19, p = .35$ | 0.25 |
| CUS 48°/s | 2.37 | 0.74 | 2.52 | 0.79 | $r = 0.59, p = .005$ | ICC = 0.58, $p < .01$ | 1.38 | $t = -0.99, df = 20, p = .33$ | −0.22 |
| Fixation *N* saccades/s | 0.01 | 0.02 | 0.008 | 0.02 | $r = 0.55, p = .02$ | ICC = 0.54, $p < .02$ | 0.04 | $t = 0.57, df = 17, p = .58$ | 0.13 |
| Antisaccade gain | −119.17 | 40.33 | −98.20 | 28.37 | $r = 0.51, p = .02$ | ICC = 0.35, $p > .10$ | 71.37 | $t = -2.69, df = 20, p = .01$ | −0.59 |
| Antisaccade spatial error | 51.72 | 26.30 | 39.62 | 9.71 | $r = 0.30, p = .18$ | ICC = 0.09, $p > .10$ | 50.26 | $t = 2.21, df = 20, p = .04$ | 0.48 |
| Antisaccade latency | 285.09 | 31.94 | 278.09 | 26.45 | $r = 0.69, p = .001$ | ICC = 0.65, $p < .01$ | 47.07 | $t = 1.36, df = 20, p = .19$ | 0.30 |
| Antisaccade error rate | 20.90 | 15.14 | 16.40 | 11.02 | $r = 0.89, p < .001$ | ICC = 0.79, $p < .01$ | 14.59 | $t = 2.83, df = 20, p = .01$ | 0.62 |
| Prosaccade gain | 102.26 | 8.39 | 98.60 | 8.02 | $r = 0.67, p = .001$ | ICC = 0.59, $p < .01$ | 13.27 | $t = 2.53, df = 20, p = .02$ | 0.55 |
| Prosaccade spatial error | 15.12 | 4.65 | 14.29 | 4.13 | $r = 0.15, p = .53$ | ICC = 0.14, $p > .10$ | 11.50 | $t = 0.66, df = 20, p = .52$ | 0.18 |
| Prosaccade latency | 183.01 | 18.80 | 187.90 | 19.13 | $r = 0.79, p < .001$ | ICC = 0.76, $p < .01$ | 24.43 | $t = -1.83, df = 20, p = .08$ | −0.40 |

**Ettinger et al 2003**

# Smooth eye pursuit deficit in schizophrenia

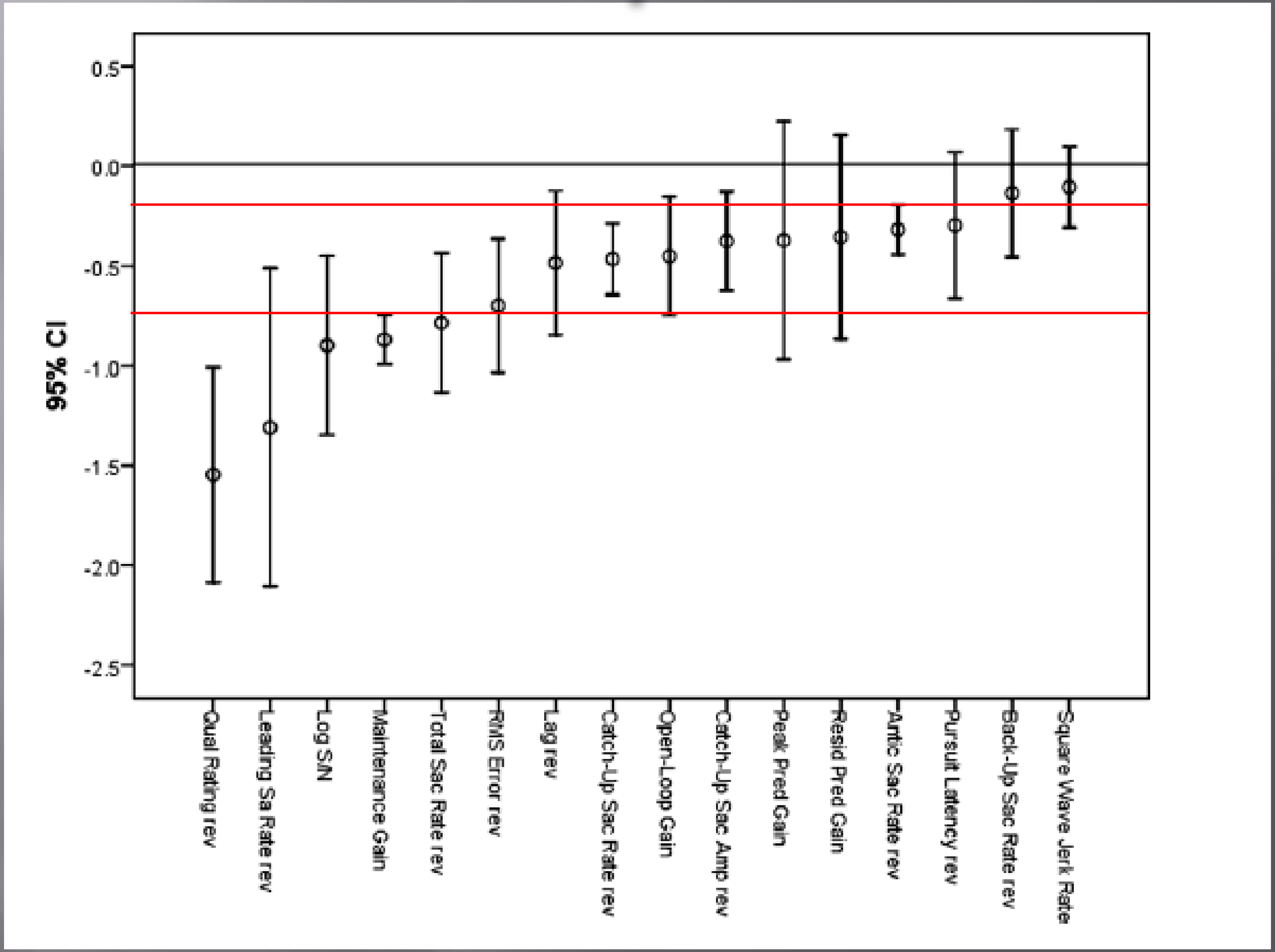
**Table 1**
Vote count for dependent variables[a]

| Variable | Studies (*n*) | Controls (*n*) | Schizophrenia (*n*) | Vote count (Sig/Nsig) |
|---|---|---|---|---|
| *Global* | | | | |
| Qualititative ratings | 9 | 196 | 244 | 9Y/0N |
| Log S/N | 4 | 123 | 168 | 4Y/0N |
| Total saccade rate | 17 | 465 | 434 | 9Y/8N |
| RMS error | 11 | 470 | 636 | 8Y/3N |
| *Pursuit system* | | | | |
| Maintenance Gain | 45 | 1471 | 1547 | 37Y/8N |
| Open loop gain/Vel/Acc | 12 | 256 | 329 | 7Y/5N |
| Pursuit latency | 8 | 203 | 242 | 3Y/5N |
| CUS rate | 26 | 899 | 985 | 11Y/16N |
| CUS amplitude | 12 | 389 | 455 | 4Y/8N |
| Resid predictive gain | 5 | 112 | 142 | 2Y/3N |
| Peak predictive gain | 5 | 178 | 158 | 2Y/3N |
| Lag | 9 | 215 | 340 | 4Y/5N |
| *Saccadic intrusions* | | | | |
| SWJ rate | 17 | 506 | 633 | 4Y/13N |
| BUS rate | 10 | 306 | 372 | 3Y/7N |
| AS rate | 22 | 795 | 831 | 9Y/13N |
| Leading saccade rate | 10 | 317 | 291 | 8Y/2N |

[a] Fifty-nine total studies were included in the vote count.

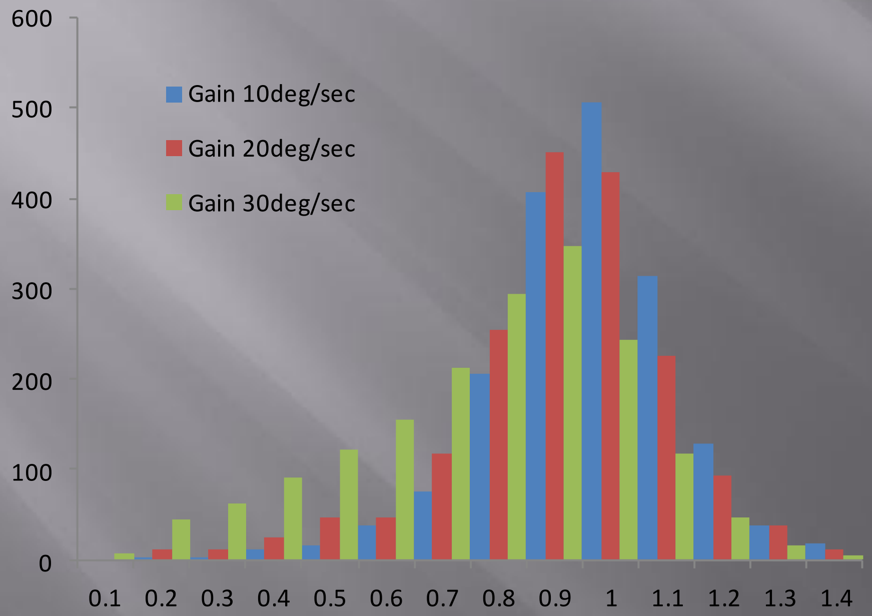
**O'Driscoll and Basso 2008**

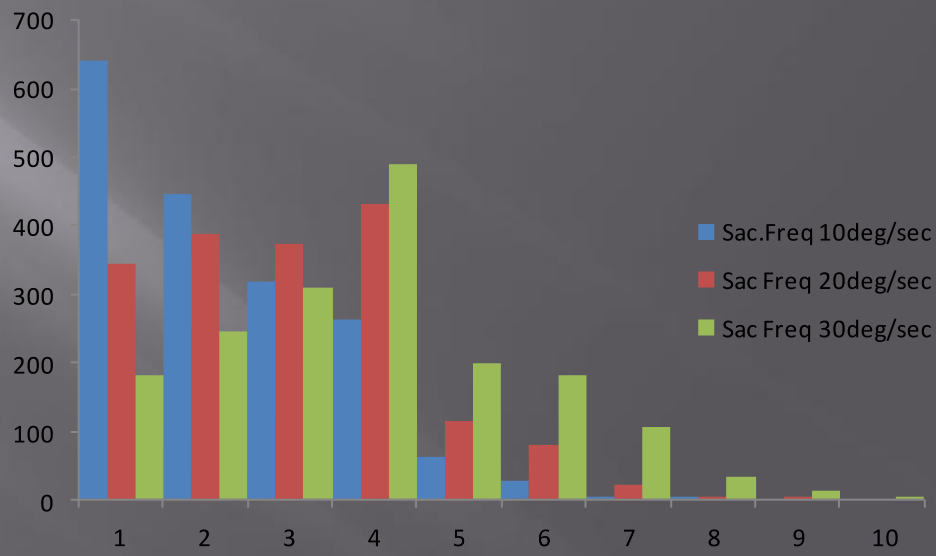
# Smooth eye pursuit deficit in schizophrenia




**O'Driscoll and Basso 2008**

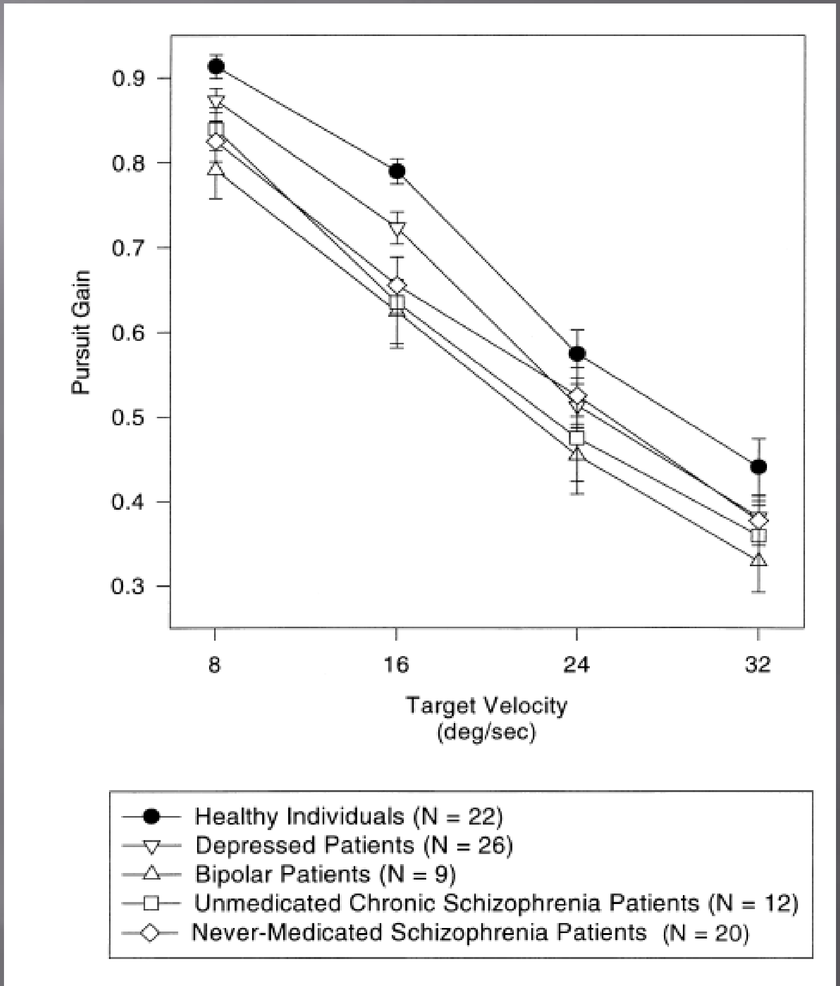
# Normal variation of smooth eye pursuit indexes in healthy young adults



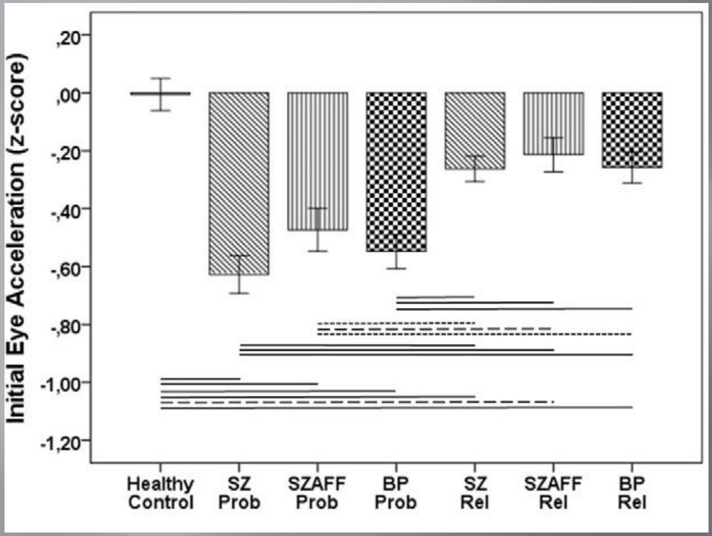

**Smyrnis et al 2007**

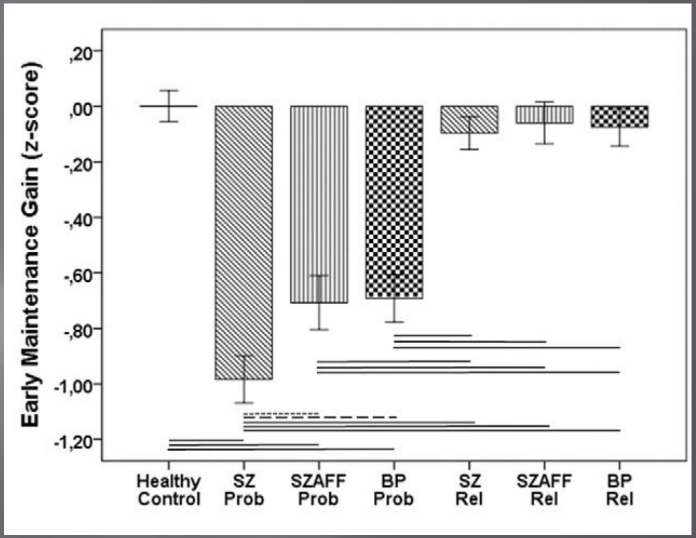
# Smooth eye pursuit in psychotic disorders



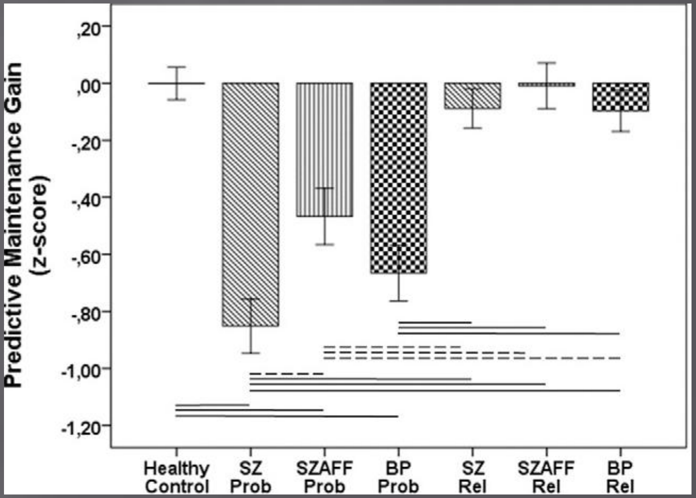

**Sweeney et al 1999**

# Smooth eye pursuit in psychotic disorders



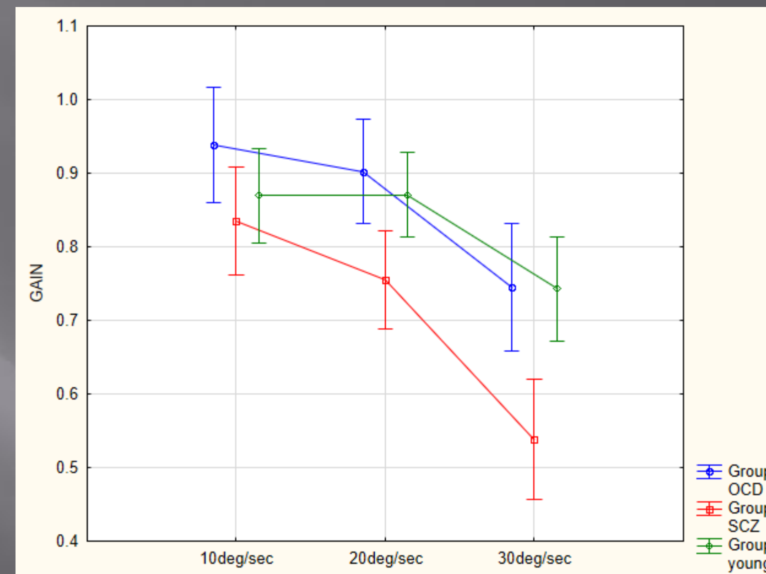

Lencer et al 2015



# Smooth eye pursuit in OCD

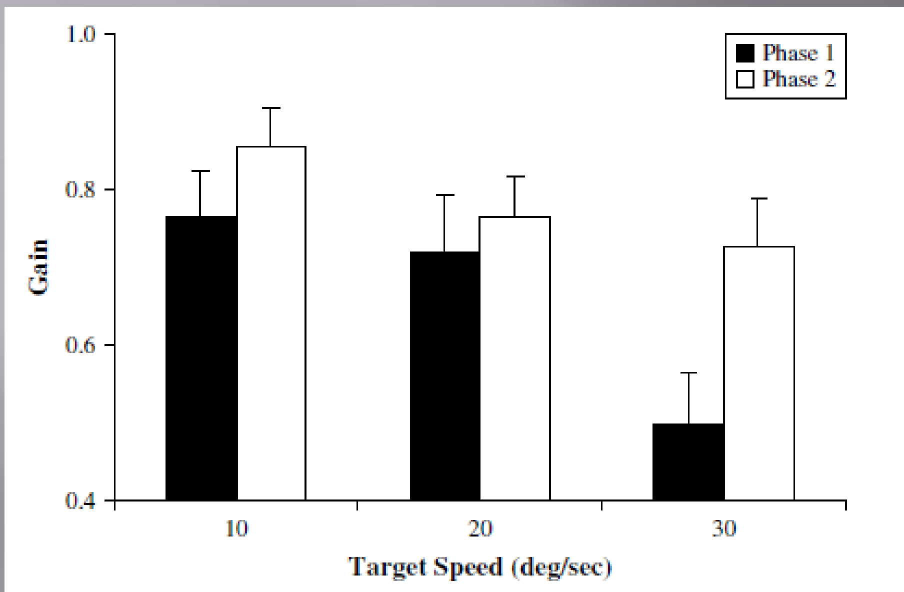
| Variable | Group | | |
|---|---|---|---|
| | Obsessive-Compulsive | Nonpsychiatric | Effect Size |
| Size (data points) | | | |
| 12 deg per sec | 4348 (803) | 4654 (503) | -0.61 |
| 24 deg per sec | 1692 (363) | 1773 (216) | -0.38 |
| Pursuit gain | | | |
| 12 deg per sec | 0.96 (0.06) | 0.97 (0.07) | -0.14 |
| 24 deg per sec | 0.91 (0.06) | 0.95 (0.05) | -0.80 |
| EyeVel sd (deg per sec) | | | |
| 12 deg per sec | 2.30 (0.59) | 2.71 (1.11) | -0.37 |
| 24 deg per sec | 3.85 (0.78) | 4.09 (1.08) | -0.22 |
| CUS frequency per sec | | | |
| 12 deg per sec | 0.69 (0.48) | 0.67 (0.52) | 0.04 |
| 24 deg per sec | 1.26 (0.70) | 0.98 (0.69) | 0.41 |
| CUS amplitude (deg) | | | |
| 12 deg per sec | 1.31 (0.34) | 1.09 (0.32) | 0.69 |
| 24 deg per sec | 2.22 (0.94) | 1.96 (0.37) | 0.70 |

Clementz et al 1996




Damilou et al 2016

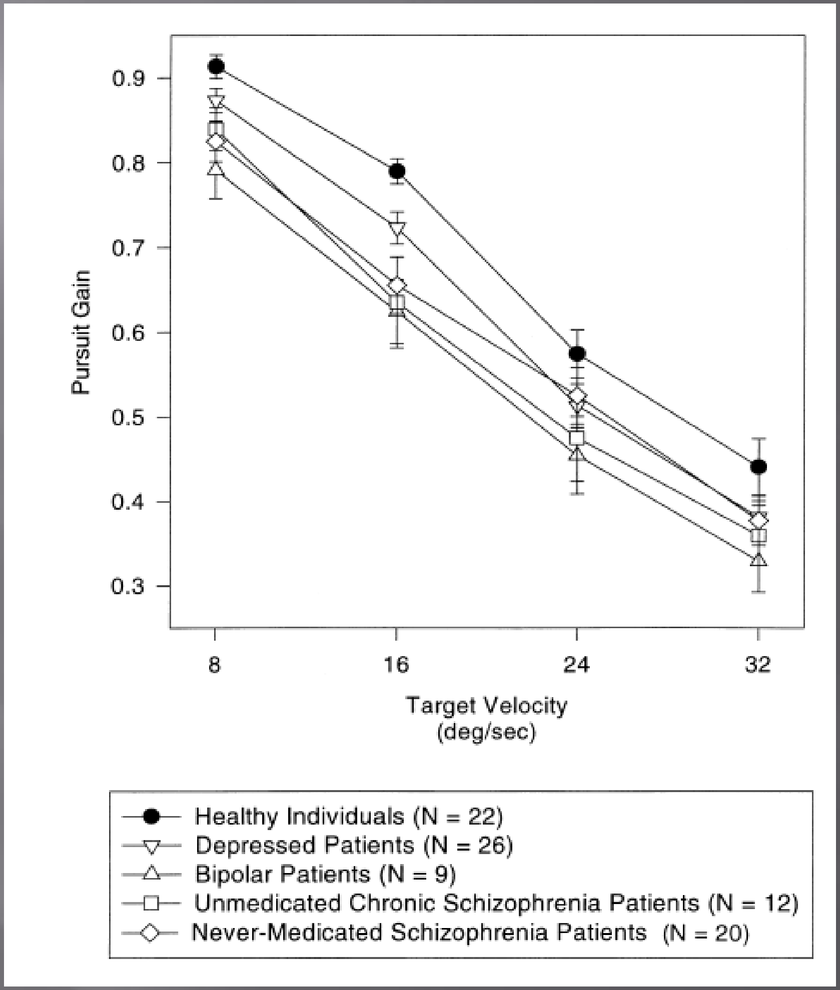
# Relation to symptom severity




| | $r^2$ | *F* | PSd *b* | *t* | NSd *b* | *t* | GSd *b* | *t* |
|---|---|---|---|---|---|---|---|---|
| *Saccade task* | | | | | | | | |
| Med latency | 0.10 | 0.6 | −0.2 | −0.62 | −0.27 | −0.88 | 0.5 | 1.32 |
| *Antisaccade task* | | | | | | | | |
| Error rate | 0.19 | 1.15 | 0.23 | 0.73 | 0.52 | 1.69 | −0.47 | −1.28 |
| Med latency | 0.07 | 0.36 | 0.13 | 0.37 | 0.33 | 0.95 | −0.36 | −0.84 |
| *Smooth eye pursuit task* | | | | | | | | |
| RMSE 10 | 0.26 | 1.93 | −0.35 | −1.21 | −0.52 | −1.85 | 0.77 | 2.26 |
| RMSE 20 | 0.06 | 0.36 | −0.17 | −0.52 | −0.02 | −0.08 | −0.08 | −0.22 |
| RMSE 30 | 0.13 | 0.82 | −0.39 | −1.23 | −0.04 | −0.14 | −0.07 | 0.18 |
| Gain 10 | 0.19 | 1.24 | 0.34 | 1.12 | 0.46 | 1.56 | −0.51 | −1.43 |
| Gain 20 | 0.53 | 2.13 | 0.25 | 0.88 | 0.63 | 2.26 | −0.43 | −1.29 |
| Gain 30 | 0.23 | 1.57 | 0.36 | 1.21 | 0.48 | 1.65 | −0.7 | −2.00 |
| Saccade frequency 10 | 0.24 | 1.66 | −0.05 | −0.16 | −0.63 | −2.2 | 0.37 | 1.07 |
| Saccade frequency 20 | 0.10 | 0.60 | 0.09 | 0.29 | −0.38 | −1.23 | 0.30 | 0.79 |
| Saccade frequency 30 | 0.08 | 0.47 | 0.02 | 0.05 | 0.18 | 0.58 | 0.12 | 0.3 |

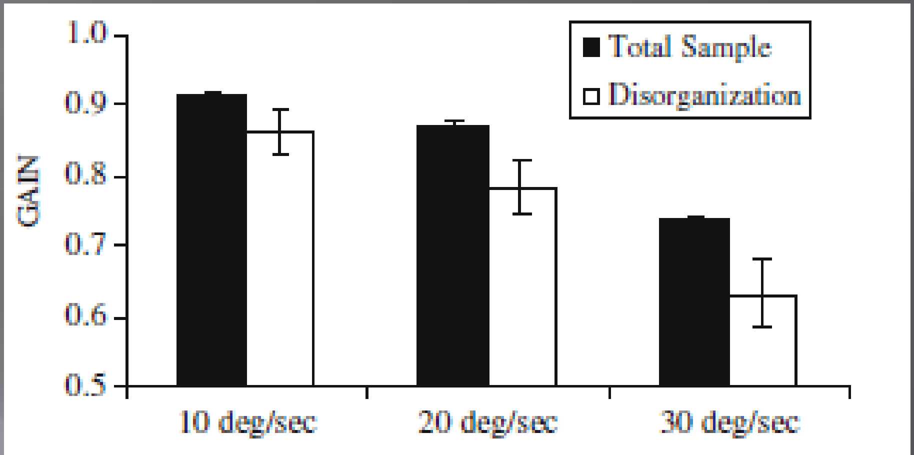
**Kallimani et al 2009**

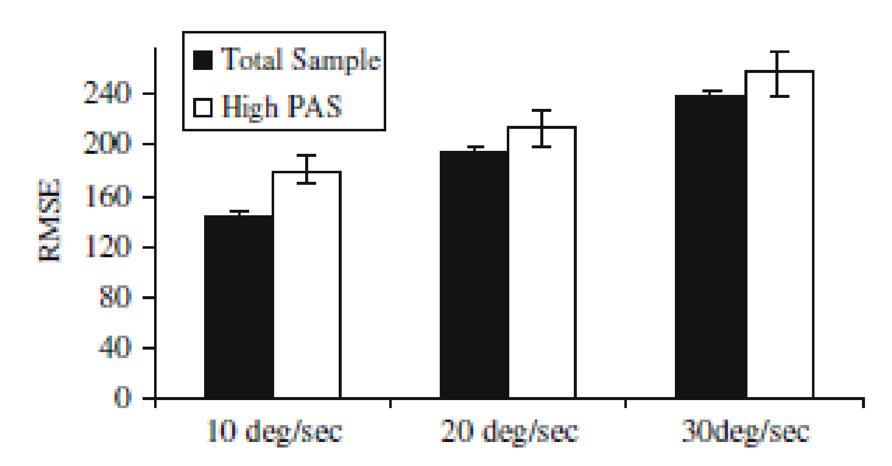
# Smooth eye pursuit deficit and medication status

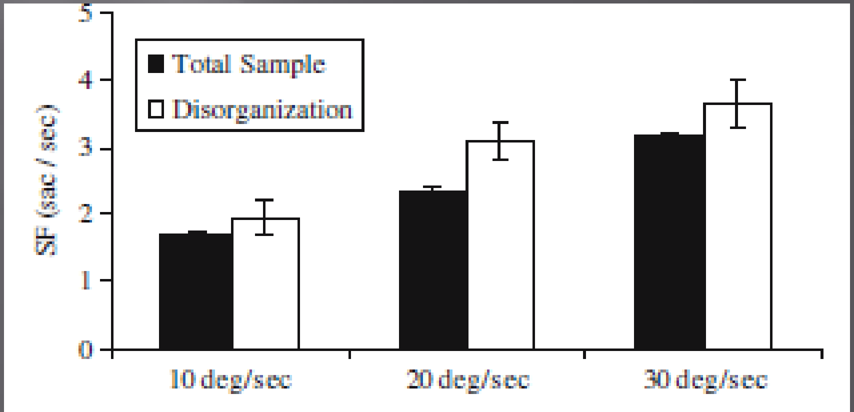



**Sweeney et al 1999**

# Smooth eye pursuit in schizotypy

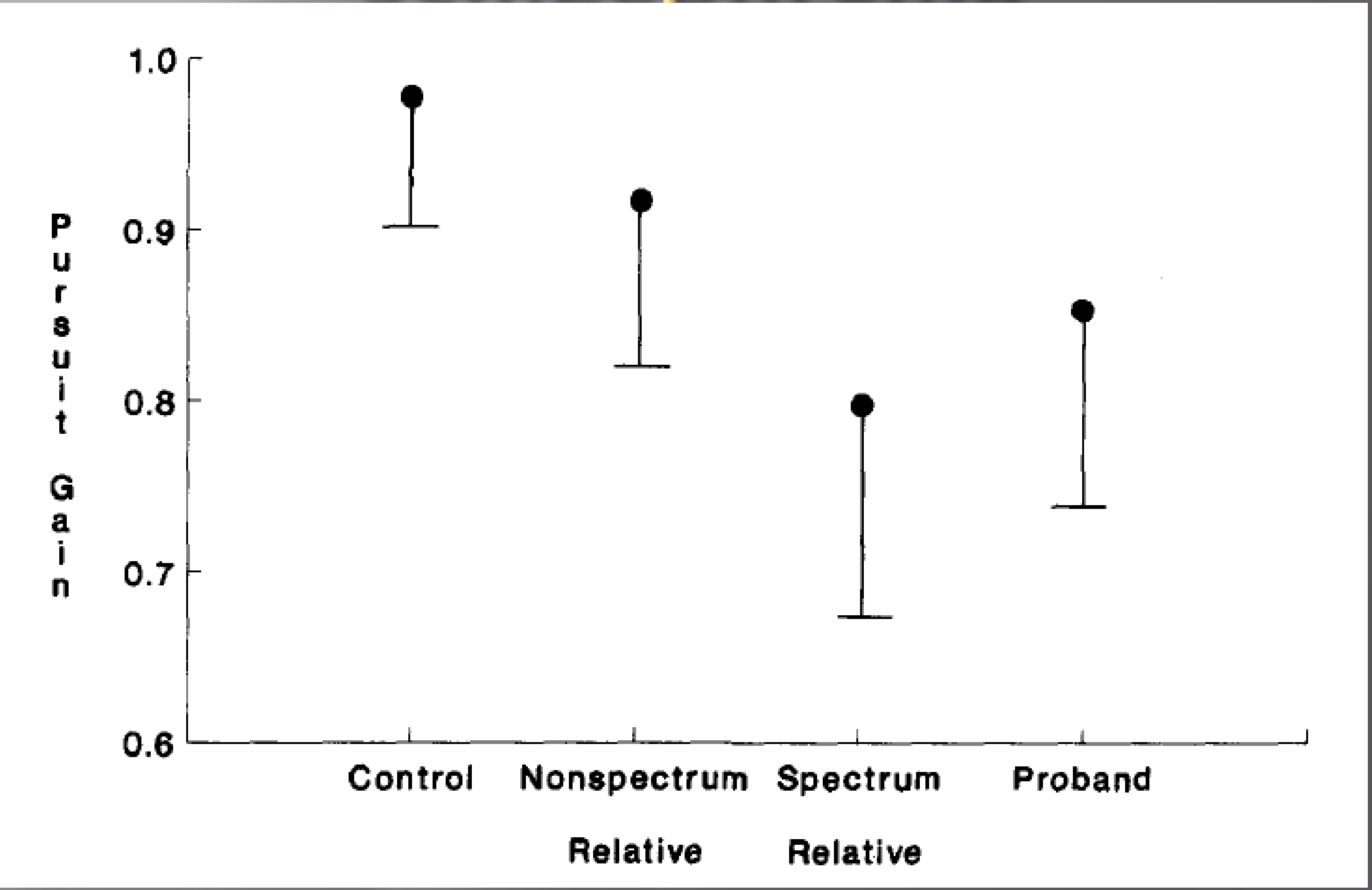


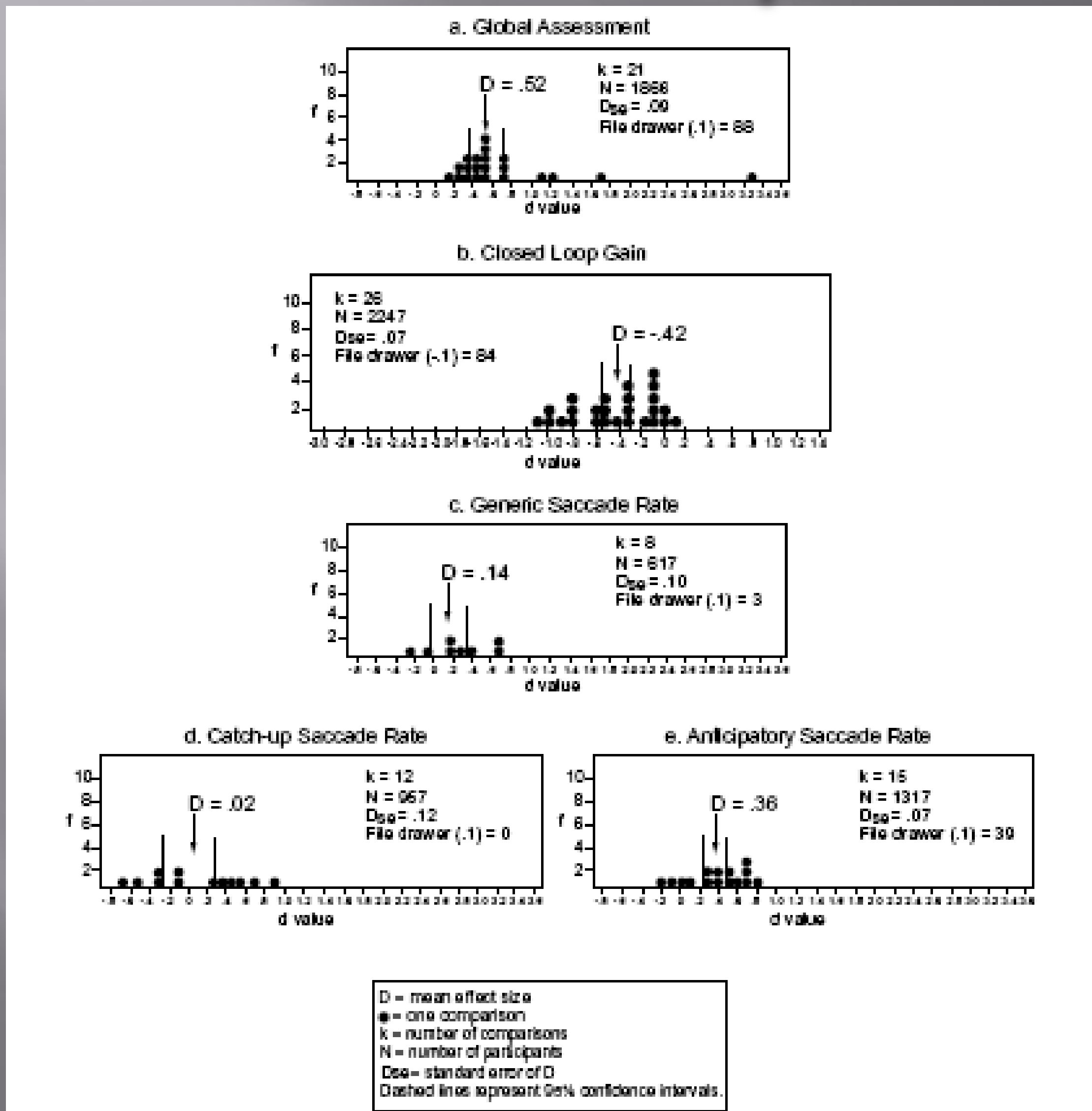

**Smyrnis et al 2007**

# Heritability of SPEM deficit in schizophrenia



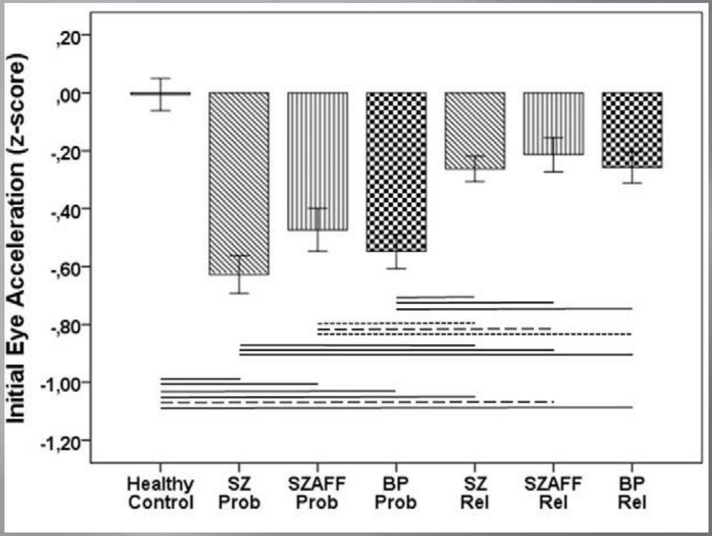

Clementz et al 1990

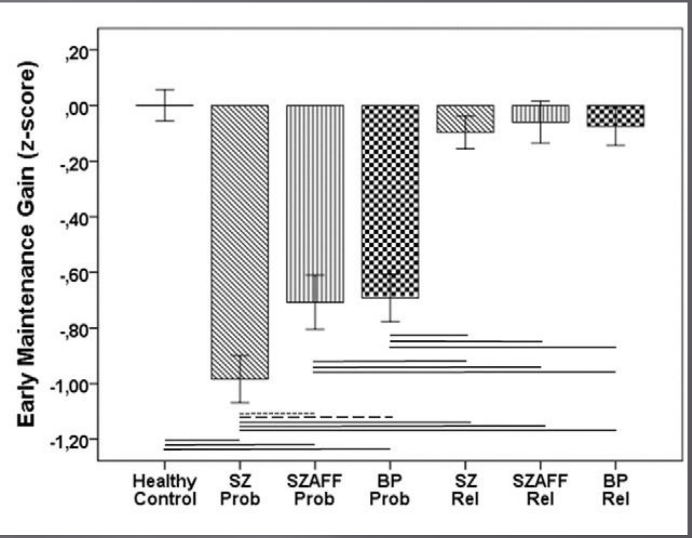
# Heritability of SPEM deficit in schizophrenia

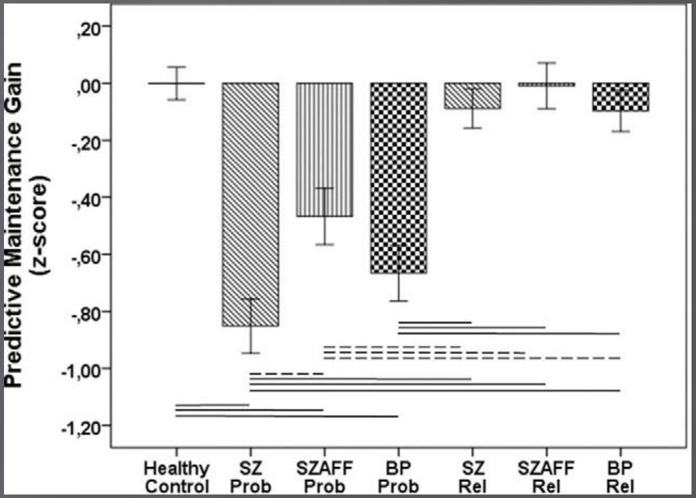



Calkins et al 2008

# Heritability of SPEM deficit in psychotic disorders




**Lencer et al 2015**

# Association of schizophrenia related GWAS SNPs to endophenotypes from ASPIS study

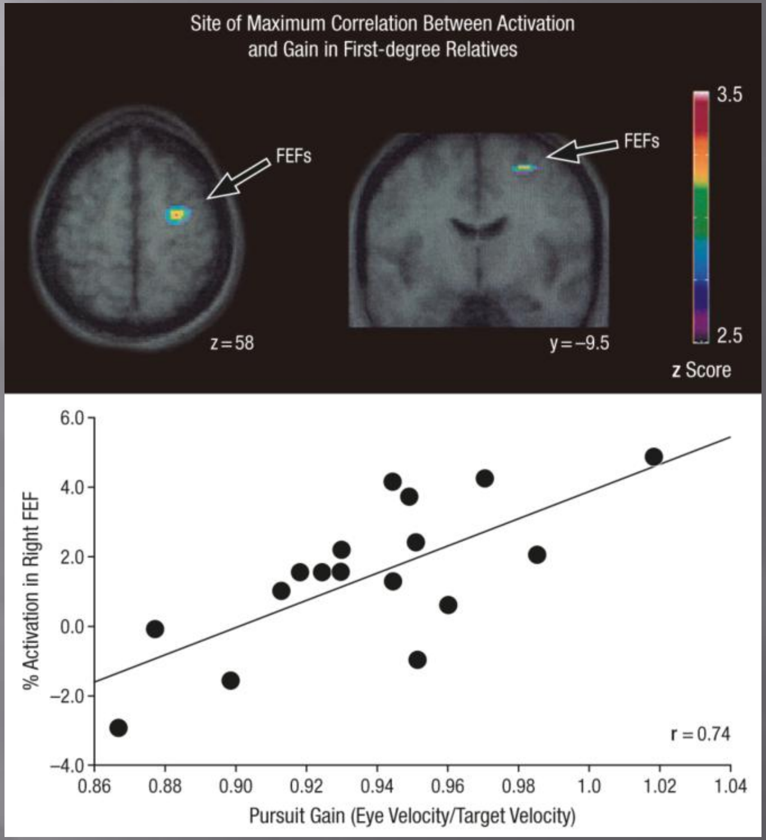
TABLE IV. PGC-SZ Genome-Wide Significant SNPs Nominally Associated With Multiple ASPIS Phenotypes

| | | ASPIS | Best ASPIS | PGC-SZ | |
|---|---|---|---|---|---|
| SNP ID | Location | Outcomes | *P*-value | *P*-value | Genes in region |
| rs12421382 | 11q22.3 | VNB, SNB | 7.8E-04 (VNB) | 3.7E-08 | C11orf87 |
| rs7523273 | 1q32.2 | CPT, ACV | 2.0E-02 (CPT) | 4.5E-08 | CD46, CR1L, CD34 |
| rs6704641 | 2q33.1 | SNB, SPEM | 7.5E-03 (SPEM) | 8.3E-09 | SATB2 |
| rs7819570 | 8q21.3 | SNB-RT, VNB-RT | 2.9E-03 (SNB-RT) | 1.2E-08 | MMP16 |
| rs4129585 | 8q24.3 | CPT-RT, SNB-RT | 7.2E-03 (CPT-RT) | 1.7E-15 | TSNARE1 |
| rs7893279 | 10p12.31 | CPT, VNB | 3.4E-02 (CPT) | 2.0E-12 | CACNB2 |
| rs77502336 | 11q24.1 | IQ, SPEM | 4.3E-03 (IQ) | 7.5E-09 | GRAMD1B |
| rs2068012 | 14q12 | VNB, SNB | 1.9E-02 (VNB) | 1.4E-08 | PRKD1, MIR548AI |

PGC, psychiatric genomics consortium.
Two-sided *P*-values are shown.

**Hatzimanolis et al 2015**

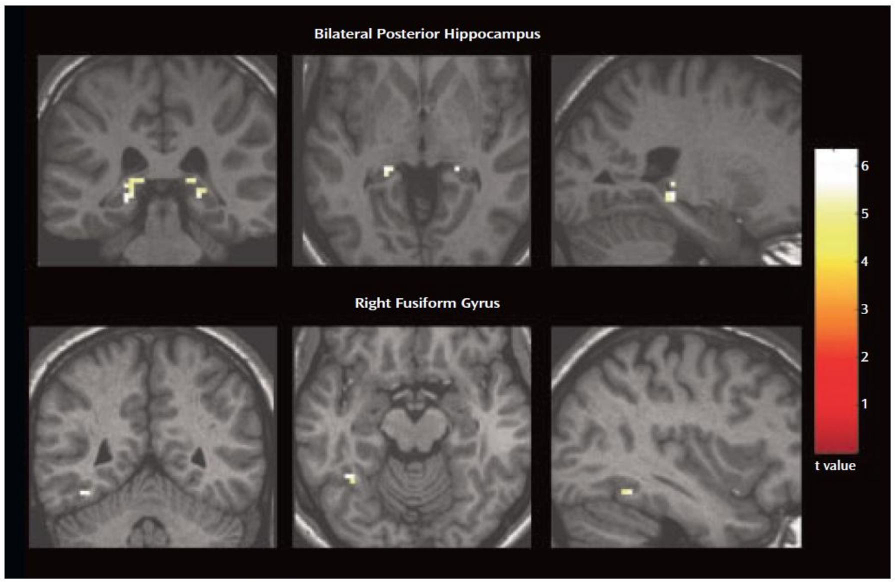
# Smooth pursuit in first degree relatives of patients with schizophrenia




O'Driscoll et al 1999

# Smooth pursuit in patients with schizophrenia vs controls

FIGURE 1. fMRI Images Showing Brain Regions in Which Subjects With Schizophrenia (N=14) Had Greater Activation During Smooth Pursuit Eye Movements Than Healthy Comparison Subjects (N=14)[a]




[a] Greater activation was found in the bilateral posterior hippocampi and right fusiform gyrus in the subjects with schizophrenia, relative to the comparison subjects. Statistical maps thresholded at $p<0.05$, corrected.

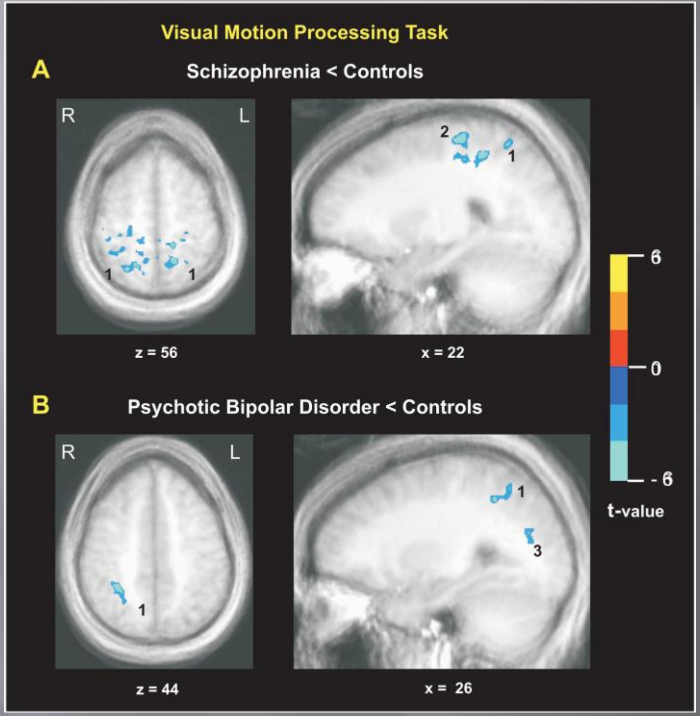
TABLE 2. Region-of-Interest Analysis Showing Less Activity During Smooth Pursuit Eye Movements in Patients With Schizophrenia (N=14) Than in Healthy Comparison Subjects (N=14)

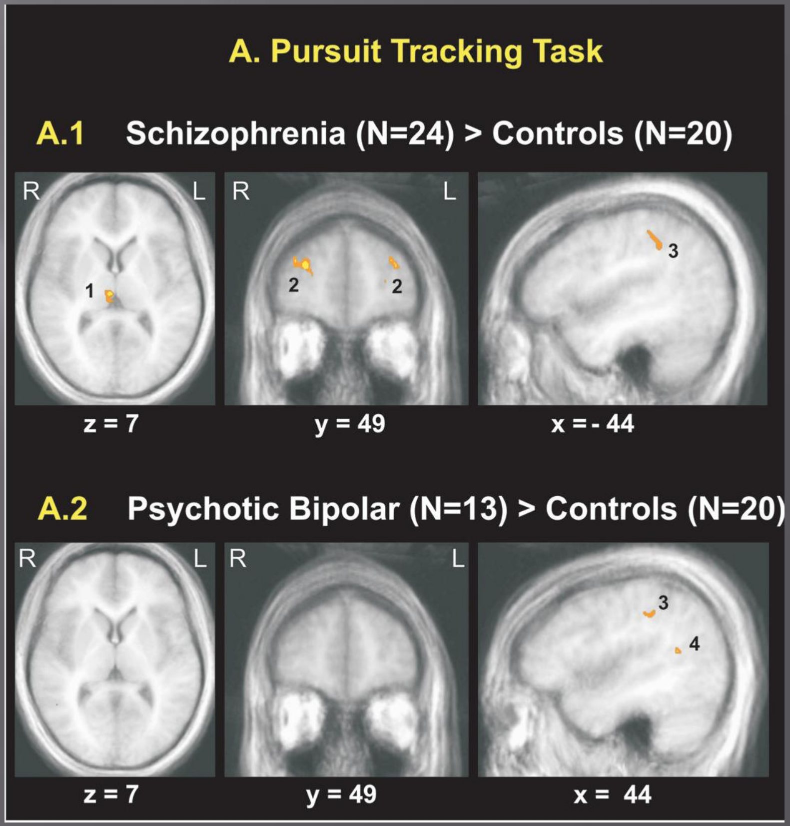
| Brain Region and Hemisphere | Location[a] | | | Significance of Difference in Activity | |
|---|---|---|---|---|---|
| | x | y | z | t | p[b] |
| Frontal eye fields, right | 51 | 3 | 39 | 2.47 | 0.04 |
| Cingulate gyrus, left | –9 | 0 | 45 | 2.45 | 0.04 |
| Medial occipital, right | 3 | –66 | 6 | 3.61 | 0.002 |

[a] Values (mm) refer to local maxima of blood-oxygen-level-dependent response at stereotactic coordinates based on dimensions of the atlas of Talairach and Tournoux (14).
[b] Bonferroni corrected for the number of regions evaluated.

**Tragellas et al 2004**

# Decreased activation of motion processing areas and increased for SPEM related areas in patients with psychotic disorders



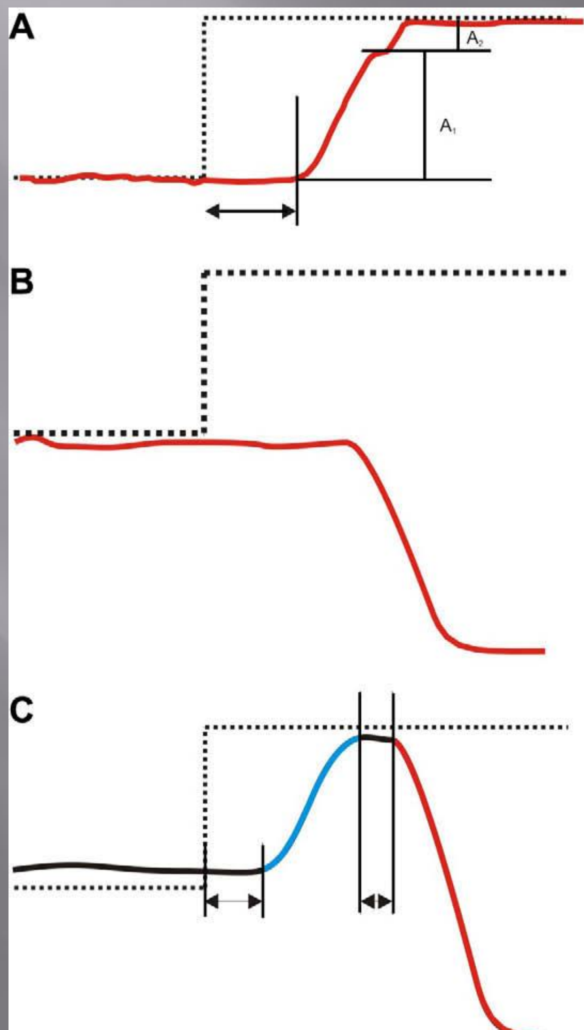




Lencer et al 2011

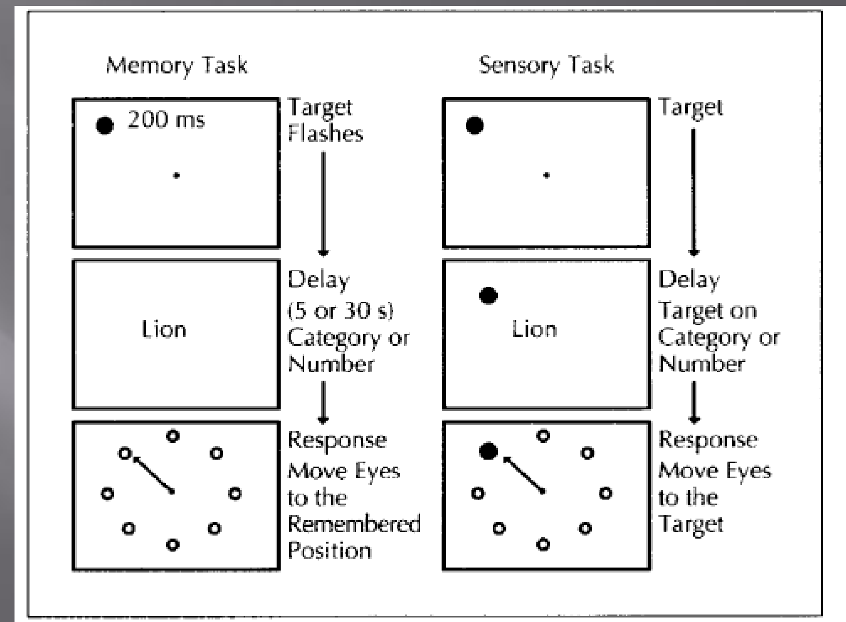
# Quiz

- 1. What is the major difference in pursuit performance between schizophrenia patients and healthy controls?
- 2. What parameters dissociate smooth pursuit performance in schizophrenia, affective disorders (bipolar, major depression) and obsessive compulsive disorder?
- 3. What parameters of smooth eye pursuit performance can be considered as endophenotypes of schizophrenia and why?
- 4. What brain areas are associated with the smooth eye pursuit deficit in schizophrenia?

# Saccadic eye movement paradigms

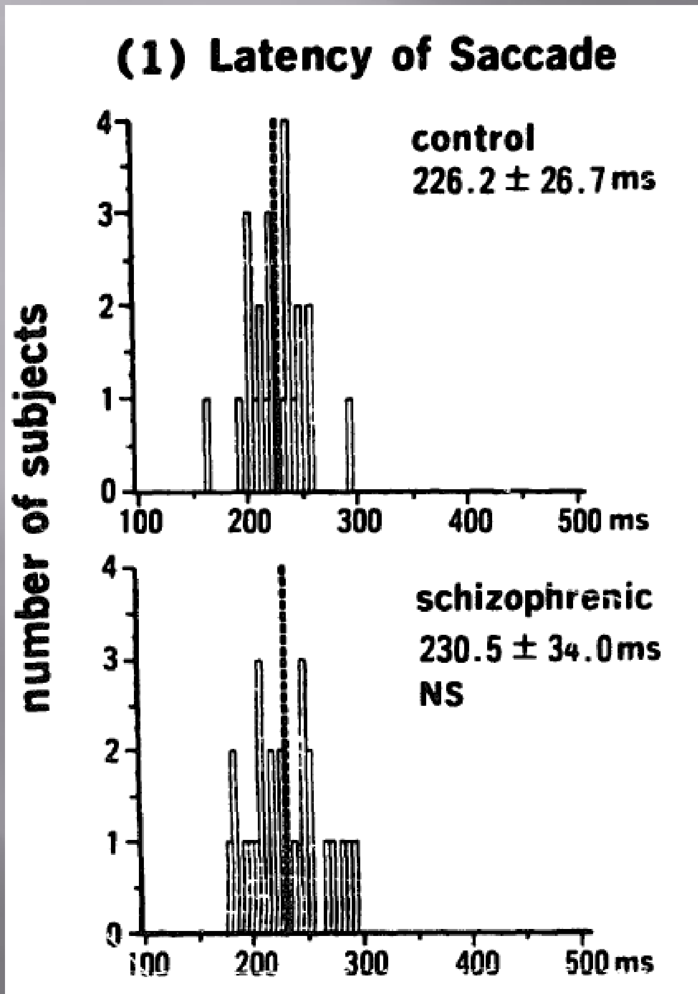



Smyrnis 2008

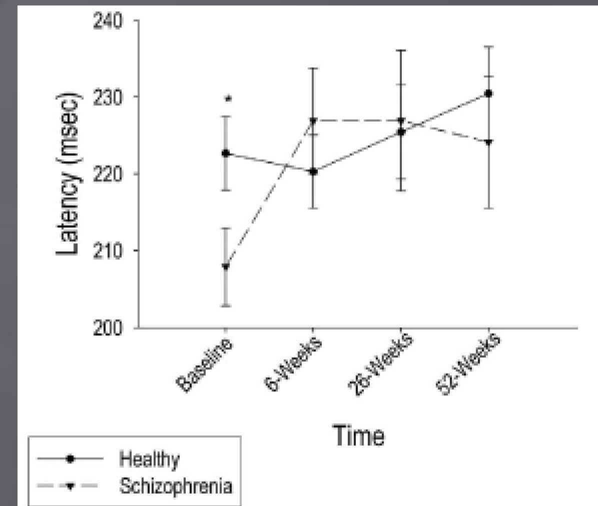



Park and Holzman 1992

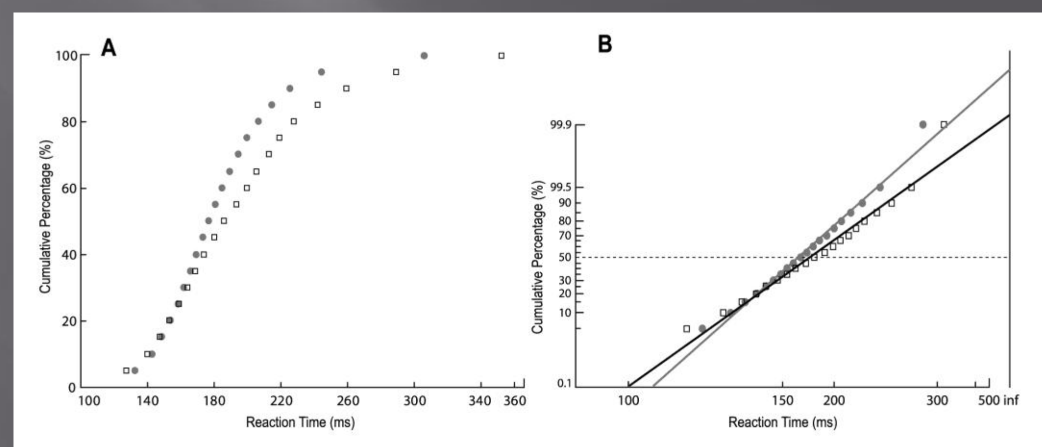
# Reflexive Saccades in Schizophrenia




Fukushima et al 1990

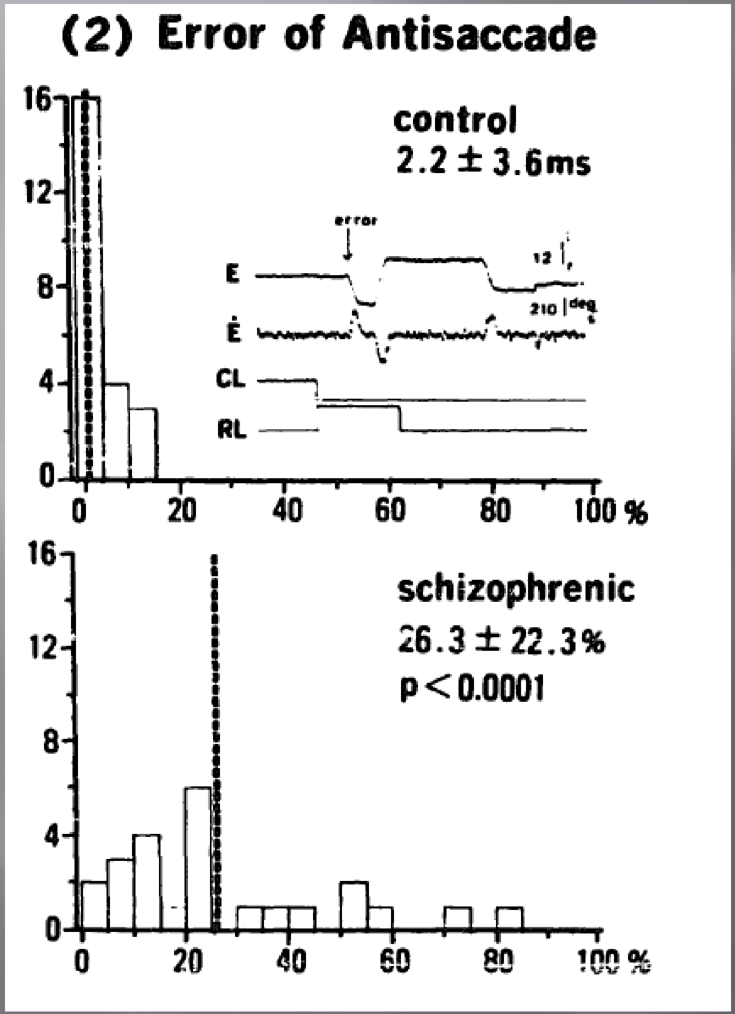


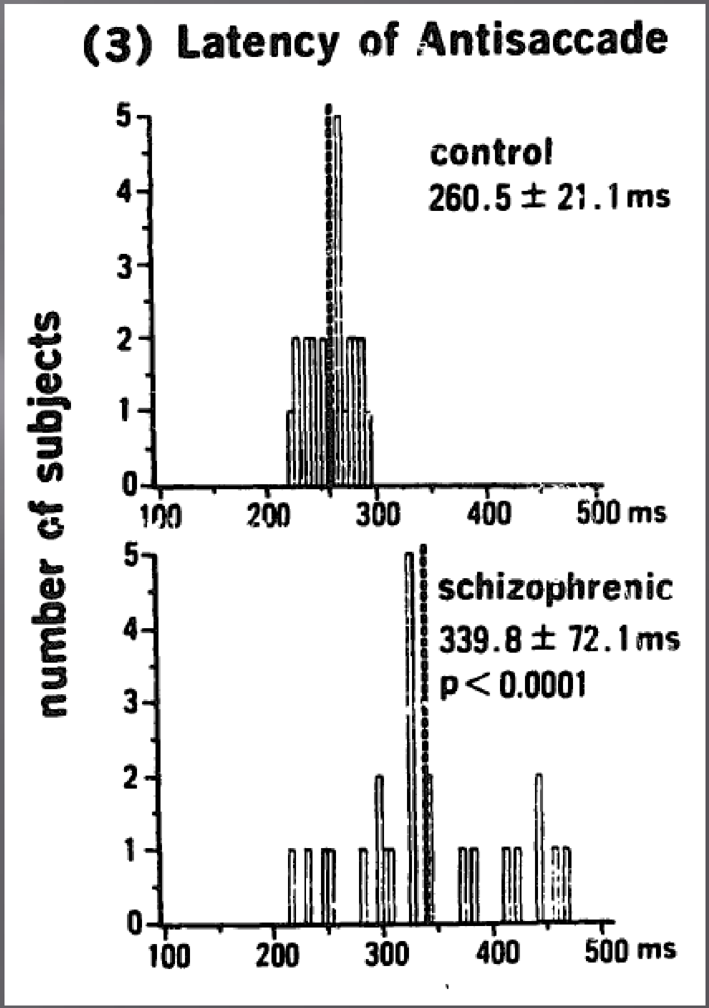

Reilly et al 2005




Smyrnis et al 2009

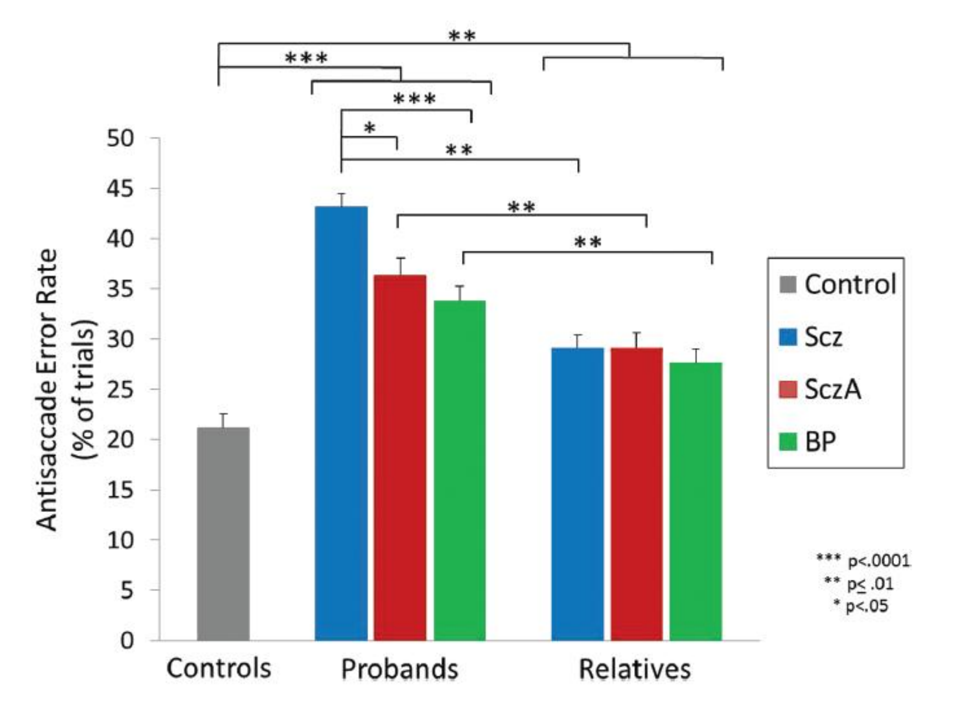
# Antisaccades in schizophrenia

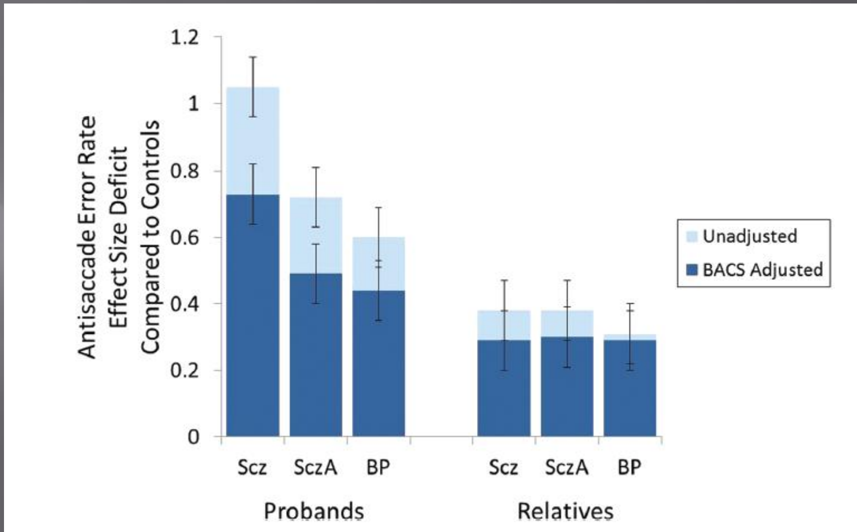



Fukushima et al 1990

# Antisaccade performance in psychosis




**Reilly et al 2014**

# Memory saccades in psychosis

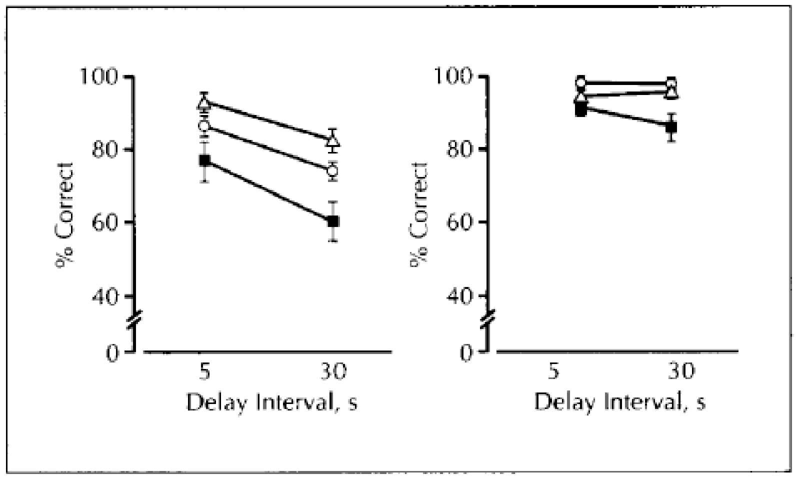



**Fig 2.**—*Percent correct eye movements to target in the memory-guided oculomotor delayed-response task (left) and in the sensory-guided oculomotor delayed-response task (right) in two delays (5 and 30 seconds) for three subject groups: schizophrenics (squares), bipolar patients (triangles), and normal controls (circles).*

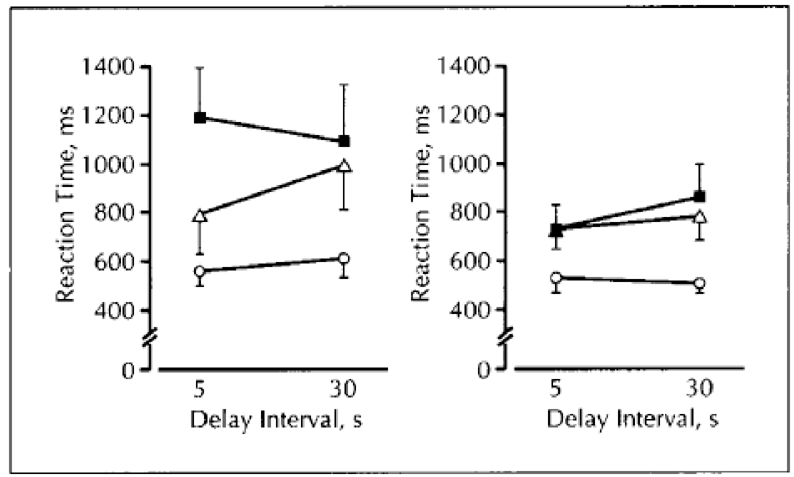



**Fig 3.**—*Reaction time for eye movements to target after two delay periods (5 and 30 seconds) in the memory-guided oculomotor delayed-response task (left) and in the sensory-guided oculomotor delayed-response task (right) for three subject groups: schizophrenics (squares), bipolar patients (triangles), and normal controls (circles).*

**Park and Holzman 1992**

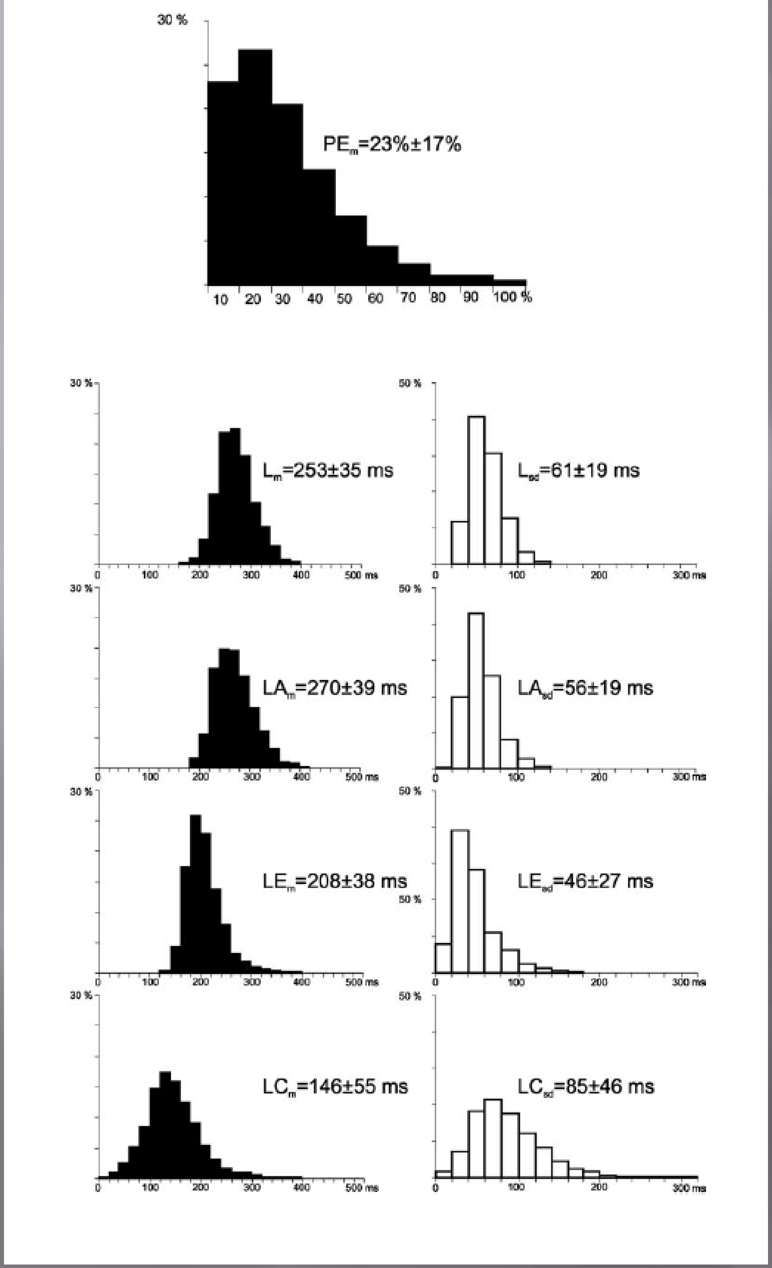
# Reliability

**Table 1.** *Descriptive Statistics of Oculomotor Variables at Baseline and Retest (N = 21), Pearson and Intraclass Correlations (ICC), Repeatability Coefficients (RC), t Tests, and Effect Sizes (ES)*

| | Baseline | | Retest | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | *SD* | Mean | *SD* | Pearson | ICC | RC | *t* test | ES |
| SPEM gain 12°/s | 98.60 | 8.09 | 96.35 | 9.28 | $r = 0.11, p = .64$ | ICC = 0.10, $p > .10$ | 23.53 | $t = 0.92, df = 19, p = .37$ | 0.19 |
| SPEM gain 24°/s | 95.32 | 10.58 | 95.89 | 11.10 | $r = 0.31, p = .17$ | ICC = 0.31, $p > .10$ | 25.45 | $t = -0.21, df = 20, p = .84$ | −0.05 |
| SPEM gain 36°/s | 89.59 | 9.03 | 88.34 | 11.77 | $r = 0.81, p < .001$ | ICC = 0.77, $p < .01$ | 14.31 | $t = 0.84, df = 19, p = .41$ | 0.18 |
| SPEM gain 48°/s | 71.85 | 16.00 | 70.34 | 14.89 | $r = 0.71, p < .001$ | ICC = 0.70, $p < .01$ | 23.71 | $t = 0.58, df = 20, p = .57$ | 0.13 |
| AS 12°/s | 0.15 | 0.21 | 0.15 | 0.19 | $r = 0.94, p < .001$ | ICC = 0.93, $p < .01$ | 0.15 | $t = 0.53, df = 19, p = .60$ | 0.02 |
| AS 24°/s | 0.40 | 0.30 | 0.44 | 0.41 | $r = 0.59, p = .005$ | ICC = 0.56, $p < .01$ | 0.68 | $t = -0.51, df = 20, p = .62$ | −0.12 |
| AS 36°/s | 0.63 | 0.36 | 0.50 | 0.32 | $r = 0.79, p < .001$ | ICC = 0.73, $p < .01$ | 0.45 | $t = 2.25, df = 19, p = .04$ | 0.57 |
| AS 48°/s | 0.50 | 0.35 | 0.44 | 0.37 | $r = 0.59, p = .004$ | ICC = 0.58, $p < .01$ | 0.65 | $t = 0.89, df = 20, p = .38$ | 0.18 |
| CUS 12°/s | 0.29 | 0.09 | 0.26 | 0.14 | $r = 0.42, p = .07$ | ICC = 0.34, $p > .10$ | 0.22 | $t = 1.82, df = 19, p = .08$ | 0.27 |
| CUS 24°/s | 1.01 | 0.39 | 0.96 | 0.27 | $r = 0.64, p = .002$ | ICC = 0.59, $p < .01$ | 0.61 | $t = 0.70, df = 20, p = .49$ | 0.17 |
| CUS 36°/s | 1.84 | 0.66 | 1.69 | 0.70 | $r = 0.60, p = .005$ | ICC = 0.58, $p < .01$ | 1.23 | $t = 0.96, df = 19, p = .35$ | 0.25 |
| CUS 48°/s | 2.37 | 0.74 | 2.52 | 0.79 | $r = 0.59, p = .005$ | ICC = 0.58, $p < .01$ | 1.38 | $t = -0.99, df = 20, p = .33$ | −0.22 |
| Fixation *N* saccades/s | 0.01 | 0.02 | 0.008 | 0.02 | $r = 0.55, p = .02$ | ICC = 0.54, $p < .02$ | 0.04 | $t = 0.57, df = 17, p = .58$ | 0.13 |
| Antisaccade gain | −119.17 | 40.33 | −98.20 | 28.37 | $r = 0.51, p = .02$ | ICC = 0.35, $p > .10$ | 71.37 | $t = -2.69, df = 20, p = .01$ | −0.59 |
| Antisaccade spatial error | 51.72 | 26.30 | 39.62 | 9.71 | $r = 0.30, p = .18$ | ICC = 0.09, $p > .10$ | 50.26 | $t = 2.21, df = 20, p = .04$ | 0.48 |
| Antisaccade latency | 285.09 | 31.94 | 278.09 | 26.45 | $r = 0.69, p = .001$ | ICC = 0.65, $p < .01$ | 47.07 | $t = 1.36, df = 20, p = .19$ | 0.30 |
| Antisaccade error rate | 20.90 | 15.14 | 16.40 | 11.02 | $r = 0.89, p < .001$ | ICC = 0.79, $p < .01$ | 14.59 | $t = 2.83, df = 20, p = .01$ | 0.62 |
| Prosaccade gain | 102.26 | 8.39 | 98.60 | 8.02 | $r = 0.67, p = .001$ | ICC = 0.59, $p < .01$ | 13.27 | $t = 2.53, df = 20, p = .02$ | 0.55 |
| Prosaccade spatial error | 15.12 | 4.65 | 14.29 | 4.13 | $r = 0.15, p = .53$ | ICC = 0.14, $p > .10$ | 11.50 | $t = 0.66, df = 20, p = .52$ | 0.18 |
| Prosaccade latency | 183.01 | 18.80 | 187.90 | 19.13 | $r = 0.79, p < .001$ | ICC = 0.76, $p < .01$ | 24.43 | $t = -1.83, df = 20, p = .08$ | −0.40 |

**Ettinger et al 2003**

# Normal variation of antisaccade indexes in young adults

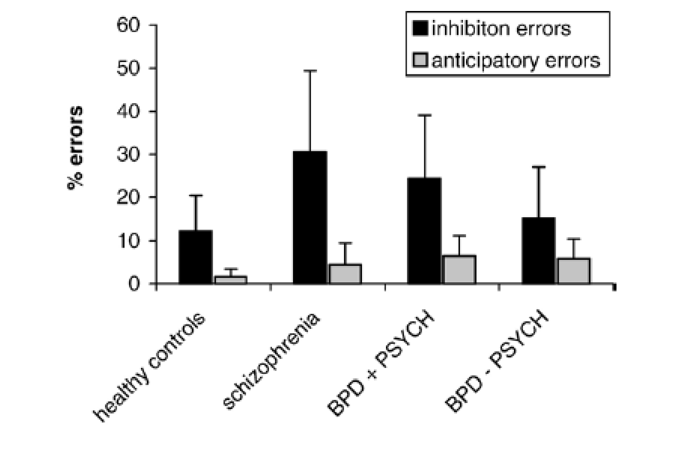



**Evdokimidis et al 2002**

# Diagnostic Specificity

| Variable | Schizophrenia (*N* = 34) Mean (SD) | Bipolar (*N* = 21) Mean (SD) | Control (*N* = 30) Mean (SD) |
|---|---|---|---|
| Gender (% male) | 58.80 | 30.00 | 53.30 |
| Age[a] | 38.35 (9.29) | 39.00 (9.54) | 35.03 (10.29) |
| Estimated IQ[b] | 102.26 (9.46) | 110.40 (5.99) | 110.97 (4.68) |
| Working Memory | | | |
| Percent correct | 68.63 (27.93) | 96.33 (4.17) | 97.89 (3.66) |
| Reaction time | 1799.75 (523.82) | 1456.86 (271.83) | 1330.58 (339.98) |
| Sensorimotor Task | | | |
| Percent correct | 97.45 (6.57) | 98.67 (5.23) | 99.56 (1.45) |
| Reaction time[c] | 633.04 (160.61) | 632.26 (233.96) | 581.56 (157.70) |
| Antisaccade task | | | |
| Error rate | .51 (.26) | .30 (.18) | .14 (.10) |
| Latency[c] | | | |
| Error response | 190.96 (34.52) | 203.87 (47.59) | 193.95 (33.49) |
| Correct response | 288.99 (57.92) | 291.35 (52.48) | 258.09 (32.91) |

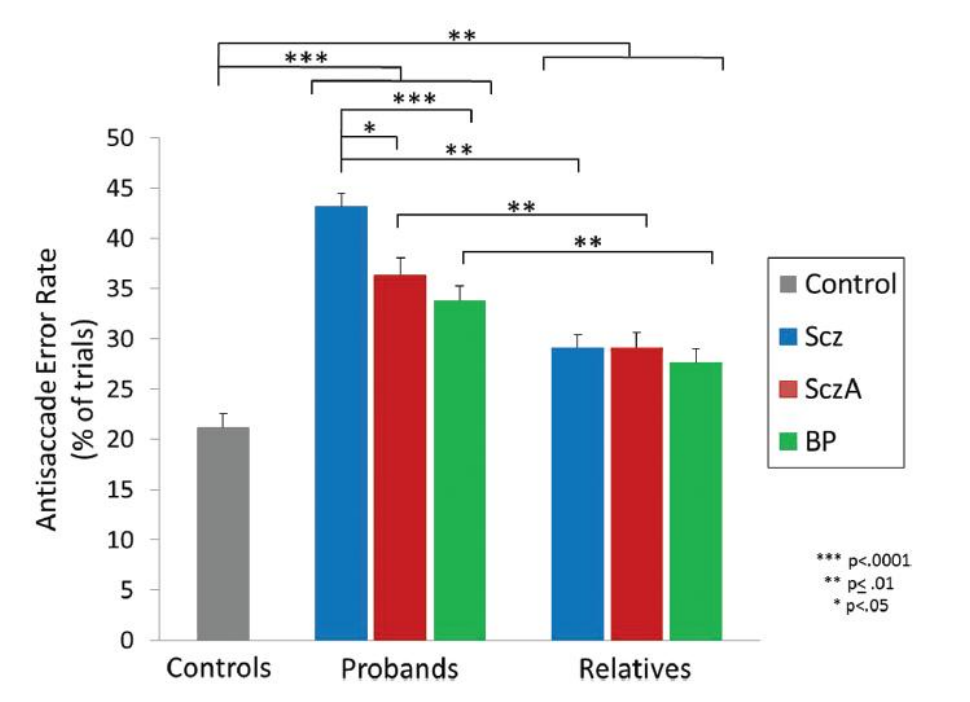
[a]Years.
[b]Estimated IQ based on the Shipley-Hartford Test.
[c]In msec.

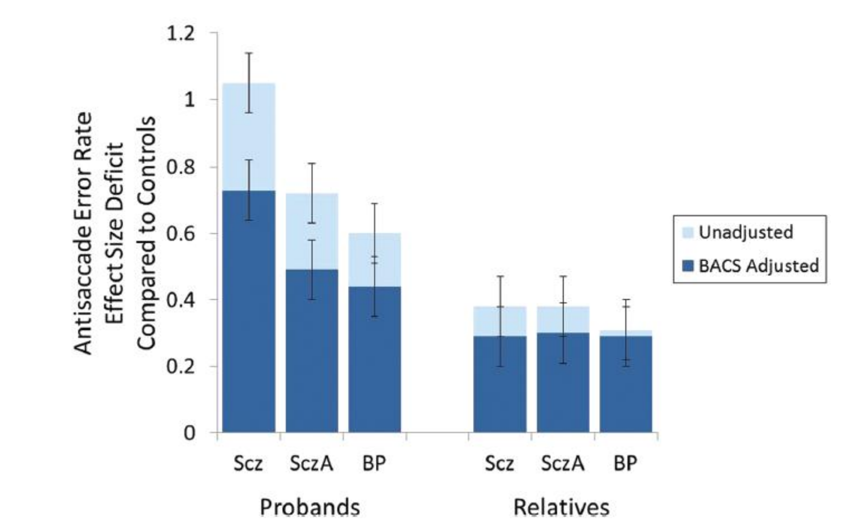



**Groutens et al 2008**

**Gouding and Tallent 2001**

# Antisaccade performance in psychosis




**Reilly et al 2014**

# Memory saccades in psychosis

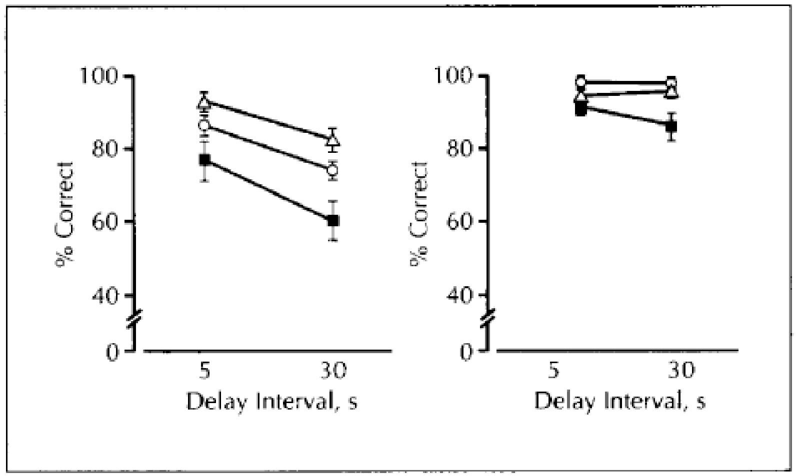



**Fig 2.**—*Percent correct eye movements to target in the memory-guided oculomotor delayed-response task (left) and in the sensory-guided oculomotor delayed-response task (right) in two delays (5 and 30 seconds) for three subject groups: schizophrenics (squares), bipolar patients (triangles), and normal controls (circles).*

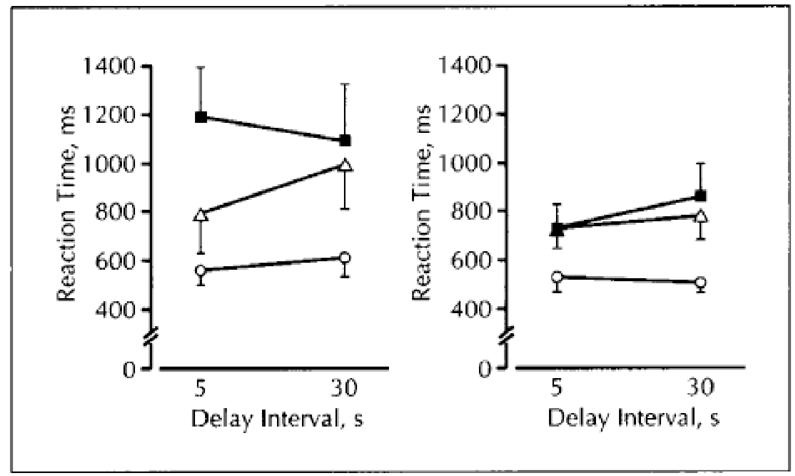
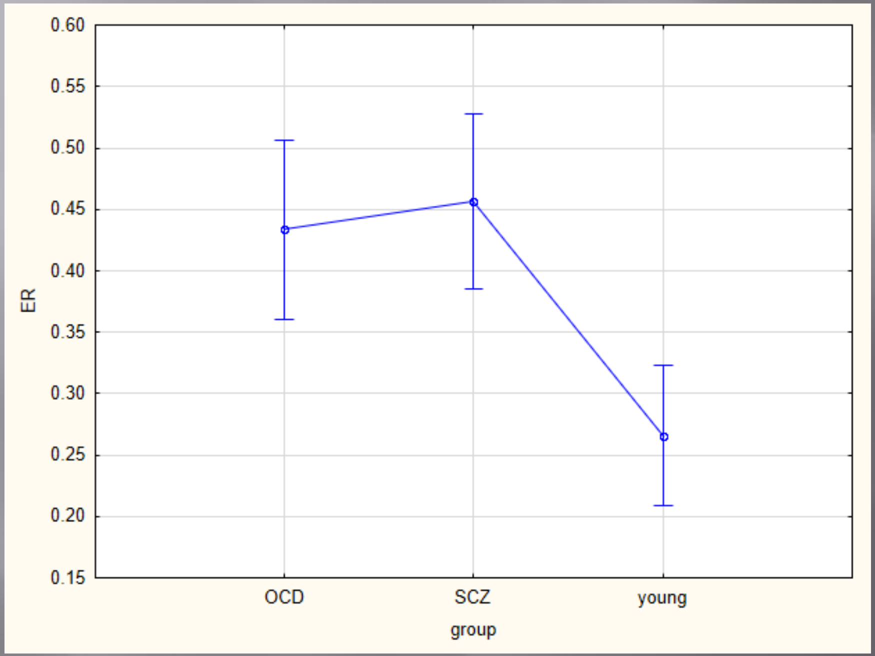
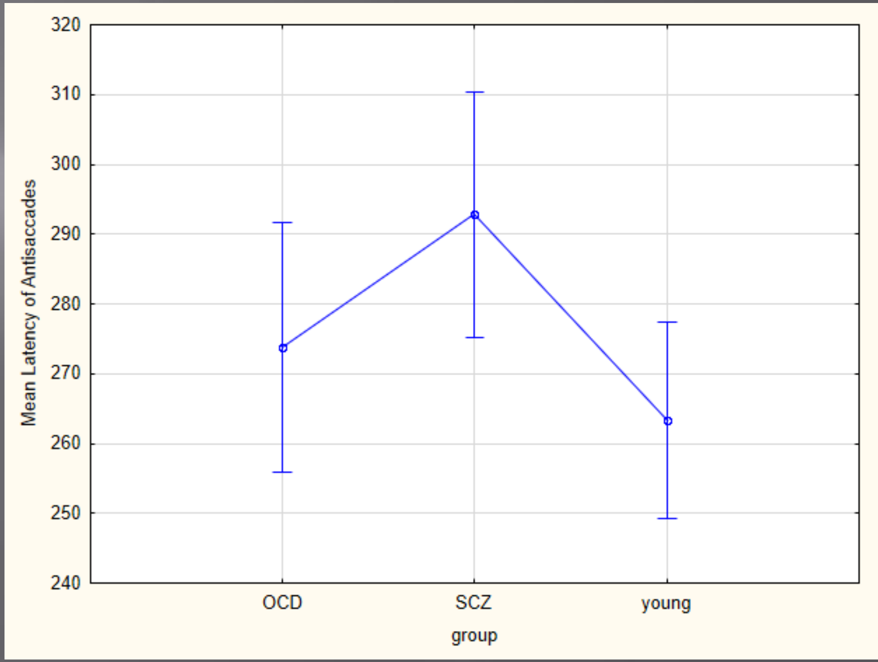



**Fig 3.**—*Reaction time for eye movements to target after two delay periods (5 and 30 seconds) in the memory-guided oculomotor delayed-response task (left) and in the sensory-guided oculomotor delayed-response task (right) for three subject groups: schizophrenics (squares), bipolar patients (triangles), and normal controls (circles).*

**Park and Holzman 1992**

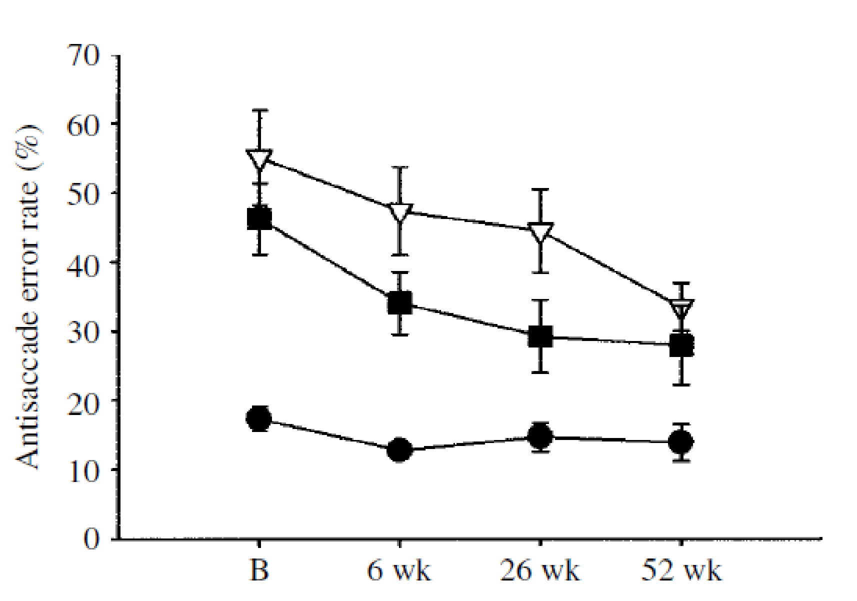
# Antisaccades in OCD

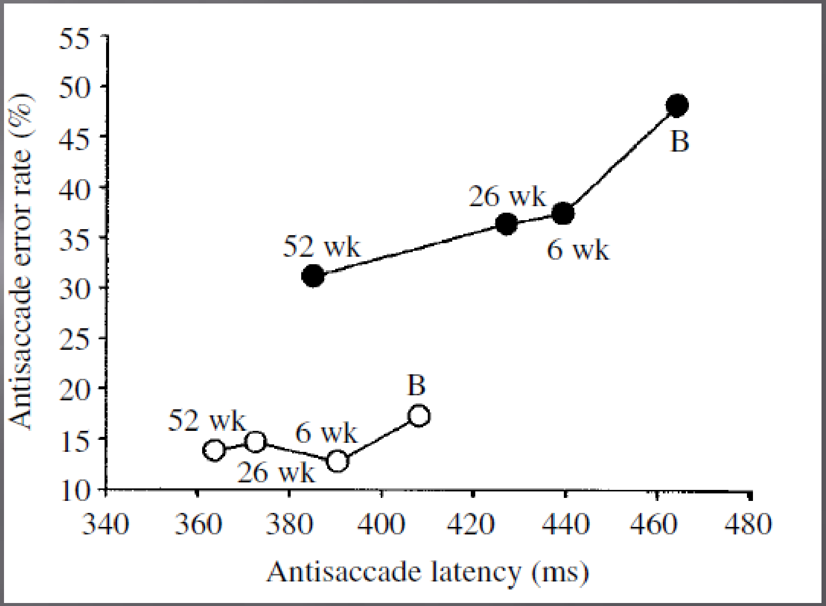



**Damilou et al 2016**

# Medication Effects and temporal stability of antisaccade deficit in schizophrenia




**Harris et al 2006**

# Relation to symptom severity

| Oculomotor variable | Phase 1 group mean (SD) | Phase 2 group mean (SD) | Paired $t_{19}$ |
|---|---|---|---|
| *Saccade task* | | | |
| Median latency (ms) | 183.5 (36.4) | 174.3 (36.6) | 1.02 |
| *Antisaccade task* | | | |
| Error rate (%) | 49.1 (29.7) | 42.8 (15.8) | 1.13 |
| Median latency (ms) | 320.4 (63.8) | 300.2 (65.6) | 1.2 |

| | $r^2$ | $F$ | PSd $b$ | $t$ | NSd $b$ | $t$ | GSd $b$ | $t$ |
|---|---|---|---|---|---|---|---|---|
| *Saccade task* | | | | | | | | |
| Med latency | 0.10 | 0.6 | −0.2 | −0.62 | −0.27 | −0.88 | 0.5 | 1.32 |
| *Antisaccade task* | | | | | | | | |
| Error rate | 0.19 | 1.15 | 0.23 | 0.73 | 0.52 | 1.69 | −0.47 | −1.28 |
| Med latency | 0.07 | 0.36 | 0.13 | 0.37 | 0.33 | 0.95 | −0.36 | −0.84 |
| *Smooth eye pursuit task* | | | | | | | | |
| RMSE 10 | 0.26 | 1.93 | −0.35 | −1.21 | −0.52 | −1.85 | 0.77 | 2.26 |
| RMSE 20 | 0.06 | 0.36 | −0.17 | −0.52 | −0.02 | −0.08 | −0.08 | −0.22 |
| RMSE 30 | 0.13 | 0.82 | −0.39 | −1.23 | −0.04 | −0.14 | −0.07 | 0.18 |
| Gain 10 | 0.19 | 1.24 | 0.34 | 1.12 | 0.46 | 1.56 | −0.51 | −1.43 |
| Gain 20 | 0.53 | 2.13 | 0.25 | 0.88 | 0.63 | 2.26 | −0.43 | −1.29 |
| Gain 30 | 0.23 | 1.57 | 0.36 | 1.21 | 0.48 | 1.65 | −0.7 | −2.00 |
| Saccade frequency 10 | 0.24 | 1.66 | −0.05 | −0.16 | −0.63 | −2.2 | 0.37 | 1.07 |
| Saccade frequency 20 | 0.10 | 0.60 | 0.09 | 0.29 | −0.38 | −1.23 | 0.30 | 0.79 |
| Saccade frequency 30 | 0.08 | 0.47 | 0.02 | 0.05 | 0.18 | 0.58 | 0.12 | 0.3 |

**Kallimani et al 2009**

# Antisaccade and schizotypy

Table 3
*Antisaccade Correlations With Schizotypy, Anxiety, and Depression*

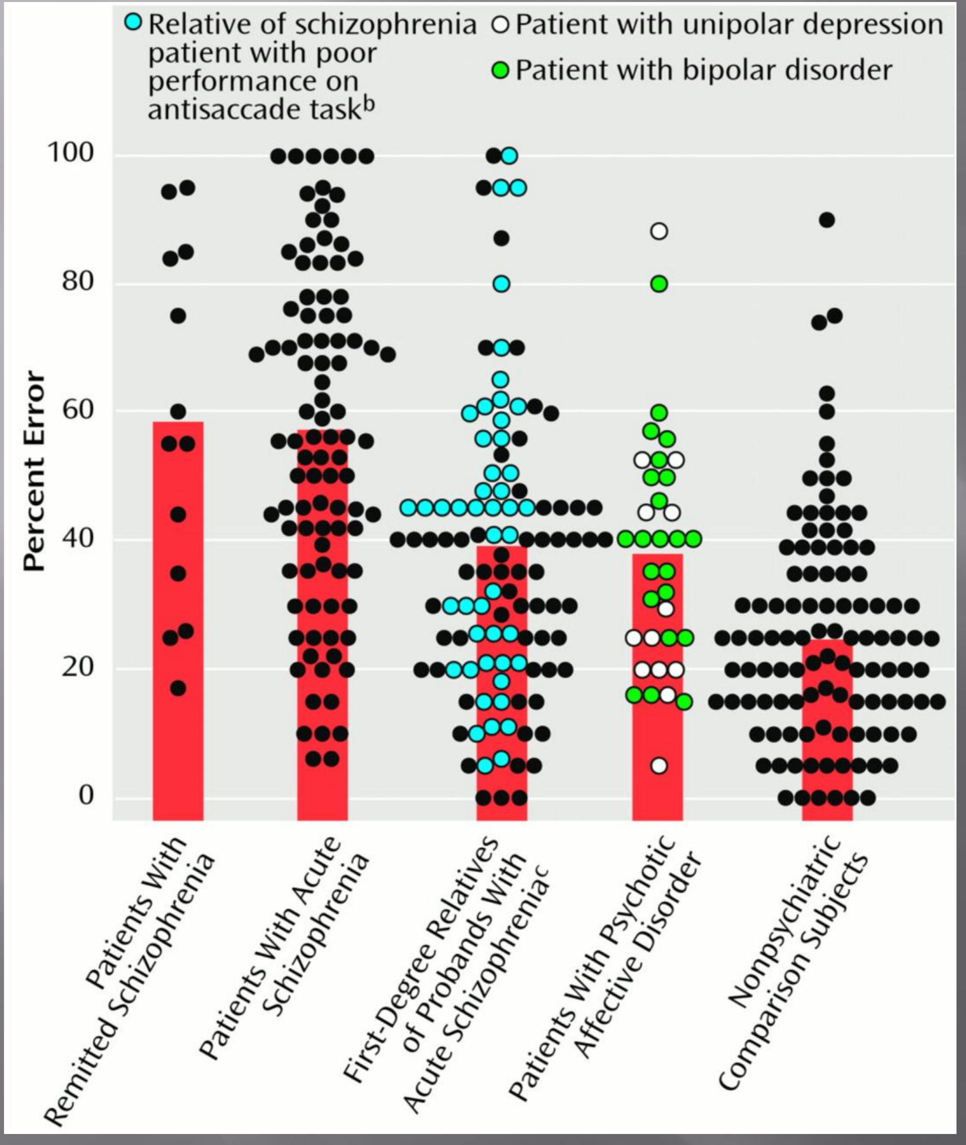
| Variable | PE(t) | $LC_M$ | $LC_{SD}$ | $LE_M$ | $LE_{SD}$ | EDU | SCL 90–R Anxiety | SCL 90–R Depression |
|---|---|---|---|---|---|---|---|---|
| PAS | .05 | .04 | .09 | .02 | .06 | −.10* | .38* | .35* |
| PAS total | .06 | .05 | .11 | .05 | .06 | −.20 | .33 | .31 |
| SPQ | .02 | .02 | .06 | .04 | .03 | −.07 | .47* | .47* |
| SPQ total | .01 | .01 | .07 | .04 | .03 | −.12 | .44 | .44 |
| F cog-per. | .00 | .01 | .04 | .02 | .04 | −.07* | .43* | .41* |
| F negative | .05 | .05 | .09 | .05 | .03 | −.10* | .35* | .37* |
| F disorganized | .02 | .02 | .06 | .04 | .03 | −.08 | .44* | .44* |
| F paranoid | −.04 | .00 | .02 | .01 | .00 | −.01 | .40* | .40* |
| SCL90–R | | | | | | | | |
| Anxiety | .08 | .02 | .10* | −.02 | .05 | .04 | — | .77* |
| Depression | .06 | −.04 | .03 | −.04 | .00 | .00 | .77* | — |

*High Perceptual Abberation Scale (PAS) Group Versus Population*

| Index | $M^a$ | $M$ | $SD$ | $t(1,270)$ | $t(1,260)$ |
|---|---|---|---|---|---|
| PE (%) | 22.2 | 29.9 | 20.3 | | |
| PE(t) | 0.466 | 0.555 | 0.238 | 3.08* | 2.58[b] |
| $LC_M$ | 266.7 | 277.7 | 39.4 | 2.08 | 1.99 |
| $LC_{SD}$ | 54.1 | 62.2 | 20.7 | 3.25* | 2.66* |
| $LE_M$ | 204.5 | 208.9 | 33.1 | 1.02 | — |
| $LE_{SD}$ | 44.4 | 50.2 | 25.6 | 1.86 | — |

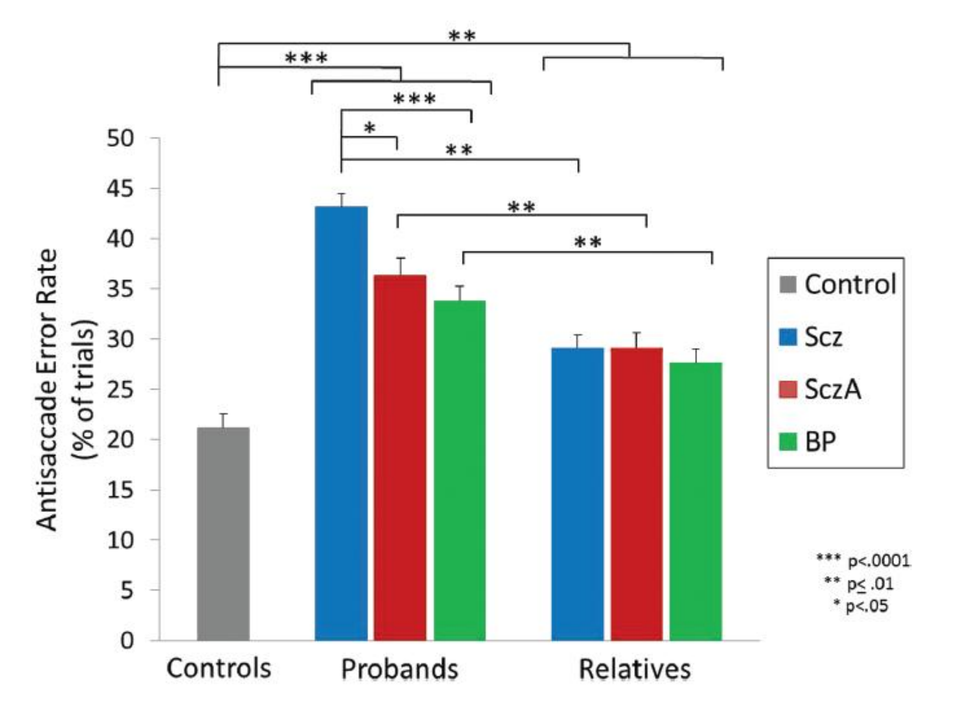
**Smyrnis et al 2003**

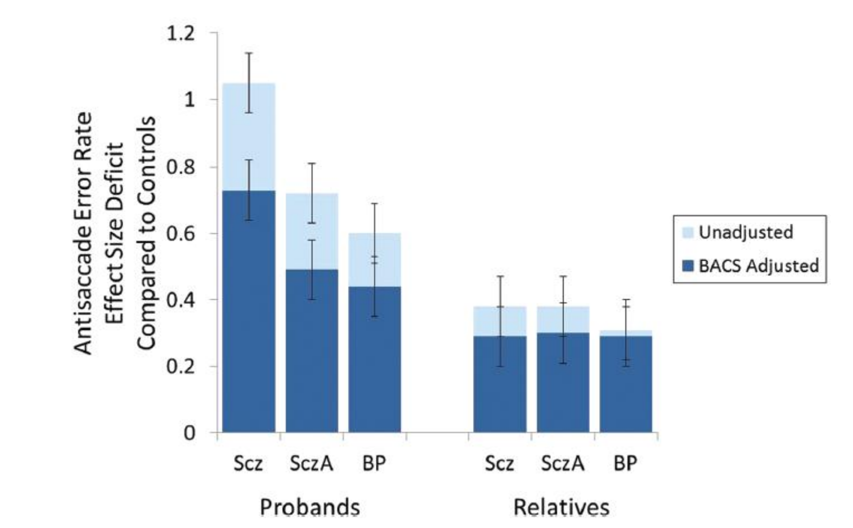
# Heritability




Curtis et al 2001

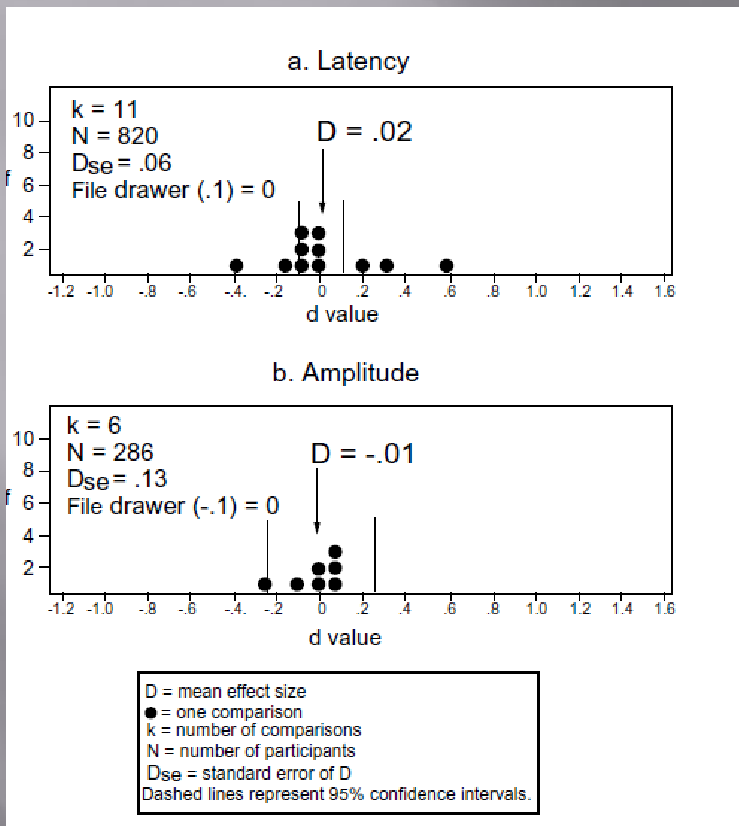
# Antisaccade performance in psychosis

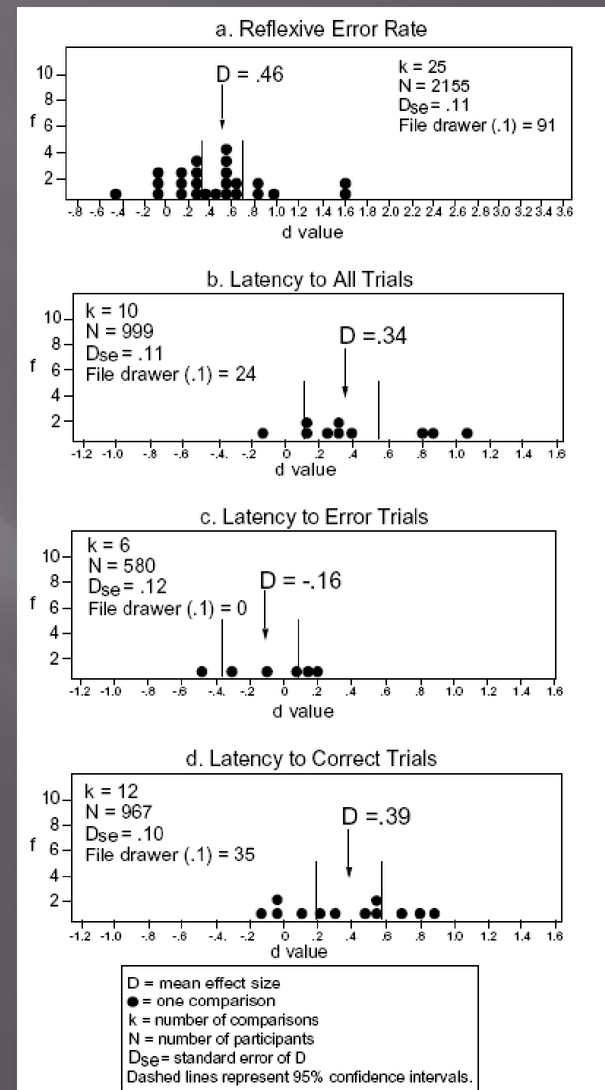



**Reilly et al 2014**

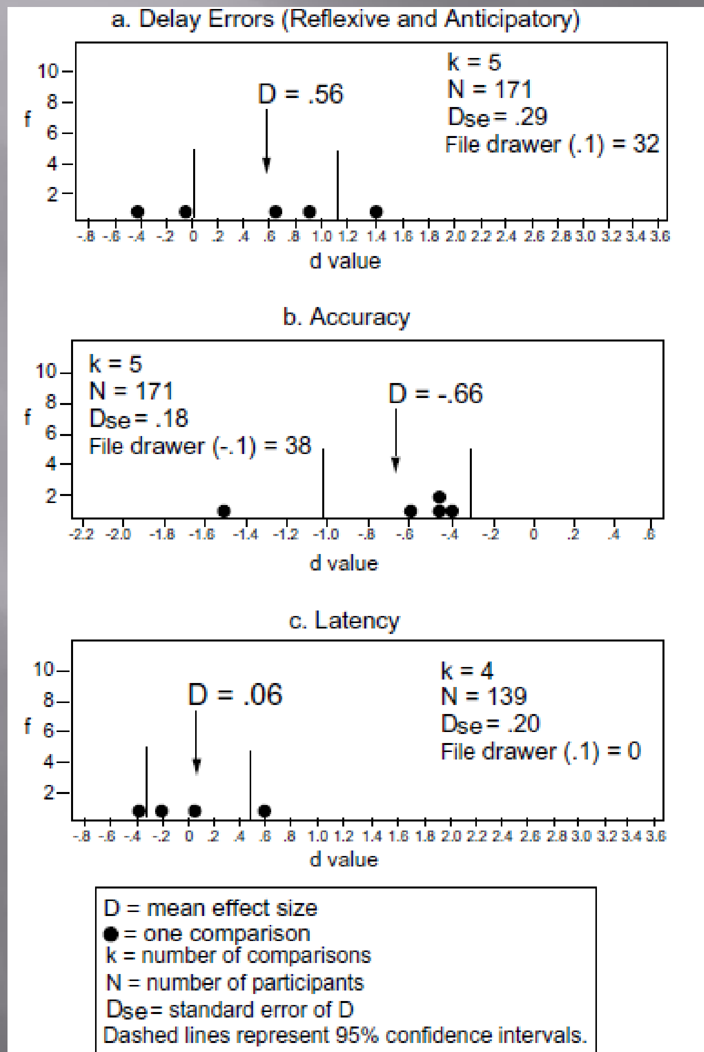
# Heritability of saccade and antisaccade deficits




**Calkins et al 2008**

# Heritability of memory saccade deficits




**Calkins et al 2008**

# Genetic associations of antisaccade measures

TABLE III. Permutation-Based Enrichment Analysis for GWAS Top-Associated Genetic Loci

| | GWAS dataset | Permuted datasets | | | | | |
|---|---|---|---|---|---|---|---|
| Outcome | $N_{obs}$ | $N_{exc}/N_{perm}$ | $P_{emp}$ | 50th PCTL | $N_{obs}$-50th PCTL | 5th PCTL | $N_{obs}$-5th PCTL |
| IQ | 391 | 11/1000 | 0.011 | 343 | 48 | 378 | 13 |
| CPT | 338 | 60/100 | ns | 342 | - | 375 | - |
| CPT-RT | 349 | 36/100 | ns | 340 | 9 | 375 | - |
| VNB | 418 | 0/3000 | <0.001 | 344 | 74 | 379 | 39 |
| VNB-RT | 323 | 84/100 | ns | 347 | - | 378 | - |
| SNB | 370 | 7/100 | ns | 343 | 27 | 373 | - |
| SNB-RT | 354 | 33/100 | ns | 345 | 10 | 383 | - |
| ERT | 357 | 25/100 | ns | 343 | 14 | 382 | - |
| ART | 381 | 35/1000 | 0.035 | 345 | 36 | 378 | 3 |
| ACV | 448 | 0/3000 | <0.001 | 352 | 96 | 387 | 61 |
| SPEM | 335 | 67/100 | ns | 345 | - | 382 | - |

$N_{obs}$, number of observed loci at GWAS $P < 0.001$.
$N_{exc}$, number of permutation where the number of loci at $P < 0.001$ exceeded $N_{obs}$.
$N_{perm}$, number of permutations performed.
$P_{emp}$, empirical $P$-value. Significant enrichment at $P < 0.05$ is shown in bold.
PCTL, percentile, for example 5th PCTL is the number of loci with $P < 0.001$ in 5% of permutations.ns, not significant ($P_{emp} > 0.05$).

**Hatzimanolis et al 2015**

# Association of schizophrenia related GWAS SNPs to endophenotypes from ASPIS study

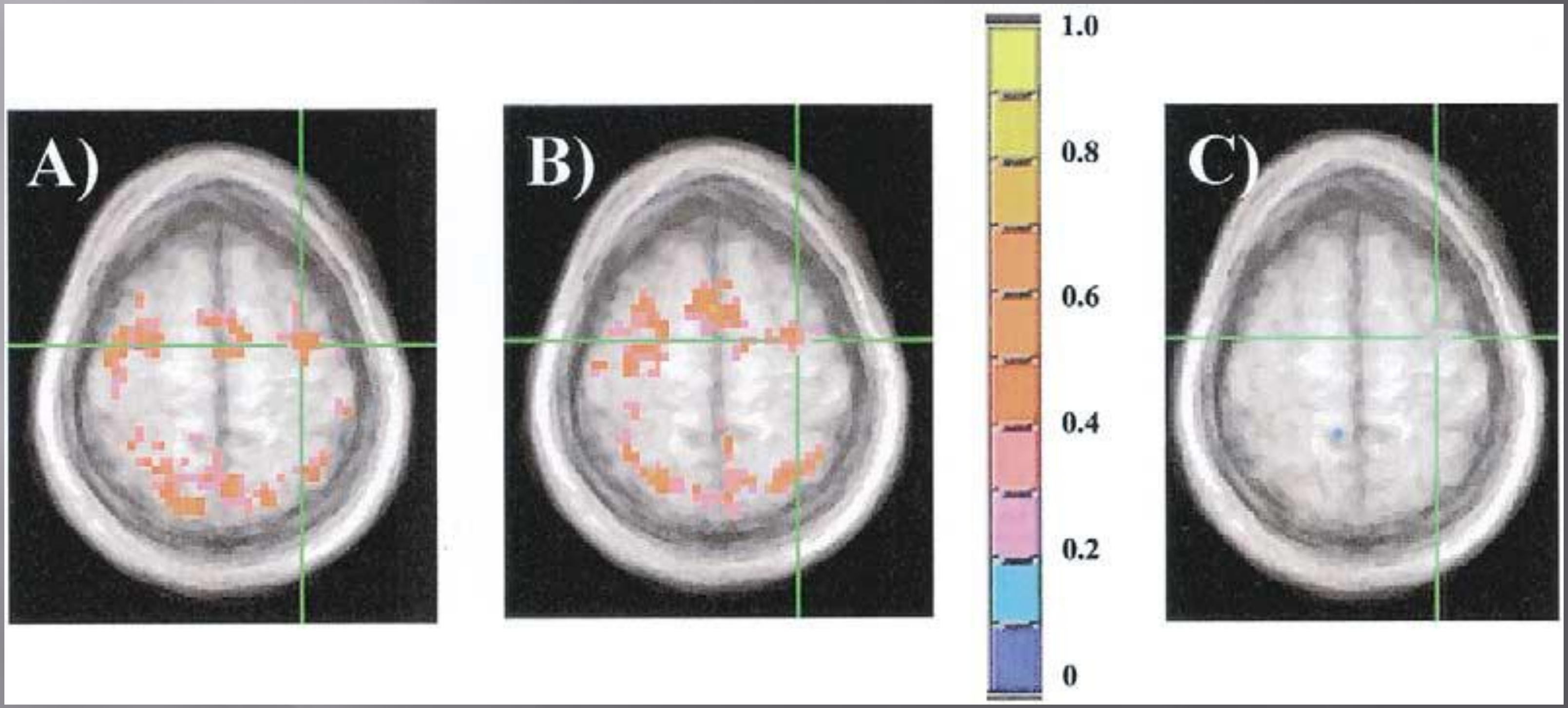
TABLE IV. PGC-SZ Genome-Wide Significant SNPs Nominally Associated With Multiple ASPIS Phenotypes

| | | ASPIS | Best ASPIS | PGC-SZ | |
|---|---|---|---|---|---|
| **SNP ID** | **Location** | **Outcomes** | ***P*-value** | ***P*-value** | **Genes in region** |
| rs12421382 | 11q22.3 | VNB, SNB | 7.8E-04 (VNB) | 3.7E-08 | C11orf87 |
| rs7523273 | 1q32.2 | CPT, ACV | 2.0E-02 (CPT) | 4.5E-08 | CD46, CR1L, CD34 |
| rs6704641 | 2q33.1 | SNB, SPEM | 7.5E-03 (SPEM) | 8.3E-09 | SATB2 |
| rs7819570 | 8q21.3 | SNB-RT, VNB-RT | 2.9E-03 (SNB-RT) | 1.2E-08 | MMP16 |
| rs4129585 | 8q24.3 | CPT-RT, SNB-RT | 7.2E-03 (CPT-RT) | 1.7E-15 | TSNARE1 |
| rs7893279 | 10p12.31 | CPT, VNB | 3.4E-02 (CPT) | 2.0E-12 | CACNB2 |
| rs77502336 | 11q24.1 | IQ, SPEM | 4.3E-03 (IQ) | 7.5E-09 | GRAMD1B |
| rs2068012 | 14q12 | VNB, SNB | 1.9E-02 (VNB) | 1.4E-08 | PRKD1, MIR548AI |

PGC, psychiatric genomics consortium.
Two-sided *P*-values are shown.

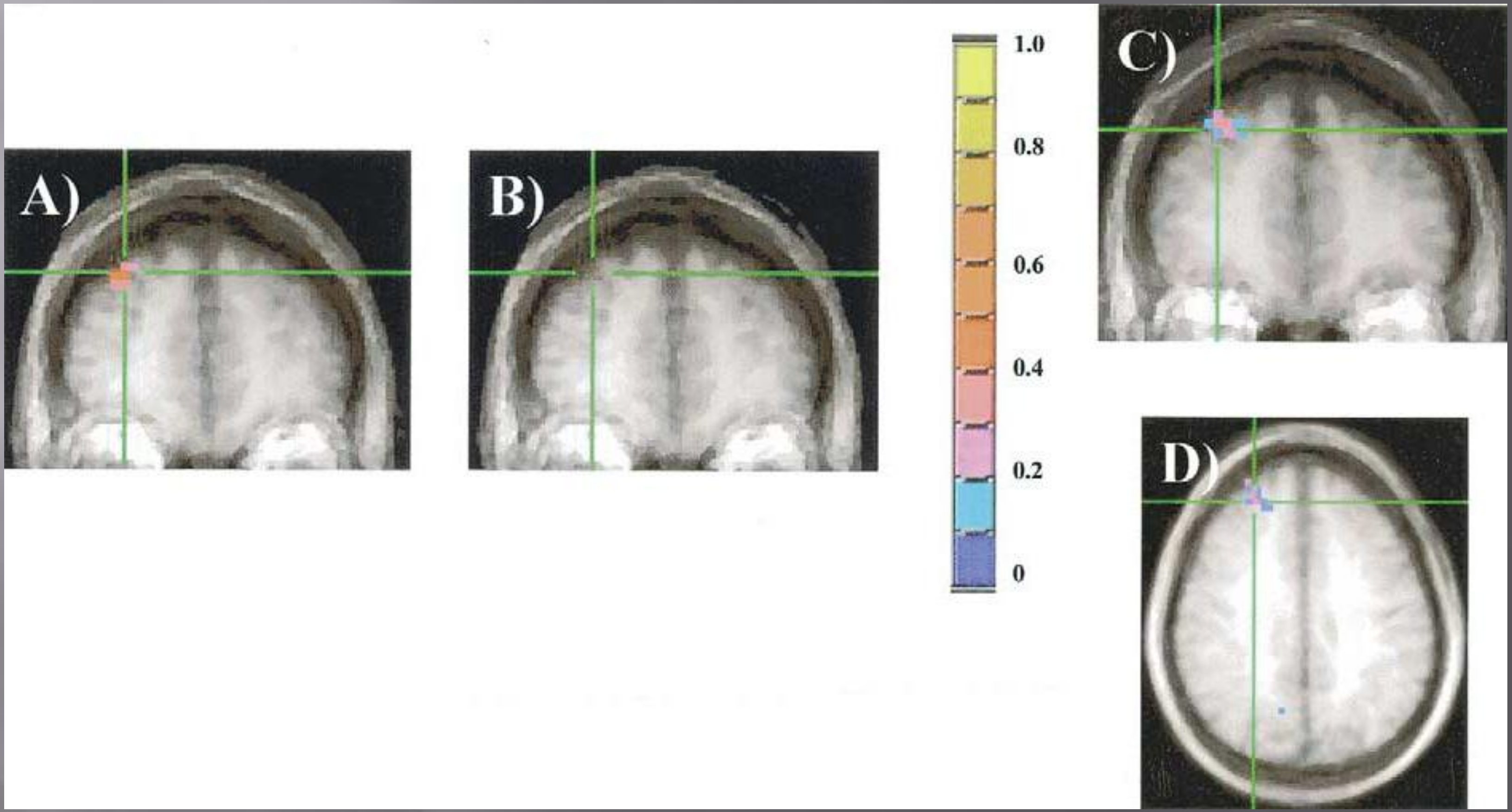
**Hatzimanolis et al 2015**

# Saccades in schizophrenia versus controls




McDowell et al 2002

# Antisaccades in Schizophrenia versus control

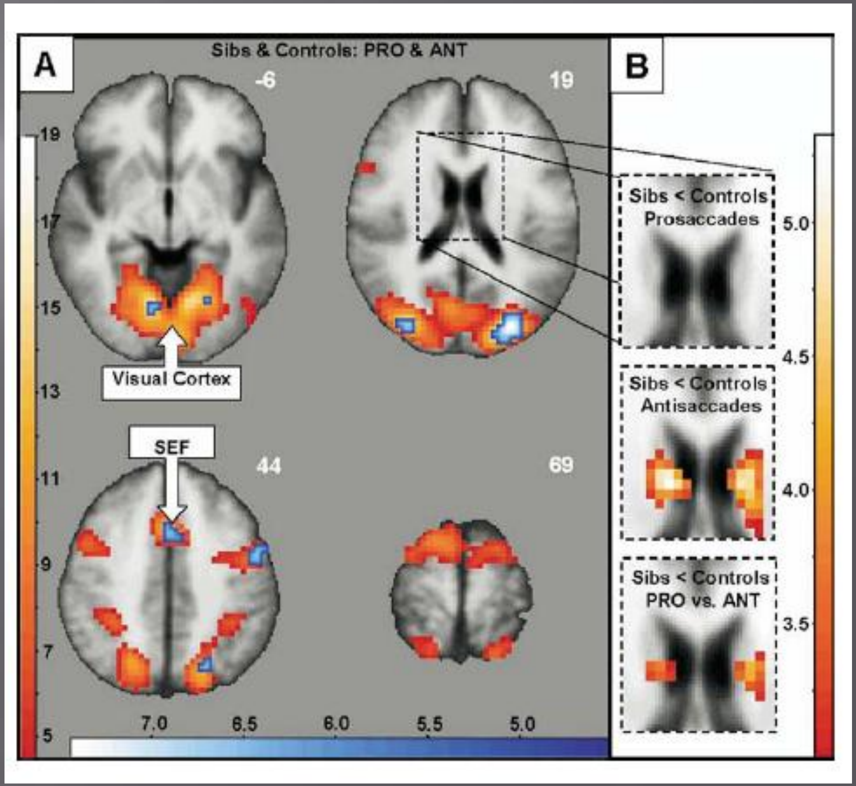



McDowell et al 2002

# Antisaccades in first degree relatives of patients with schizophrenia

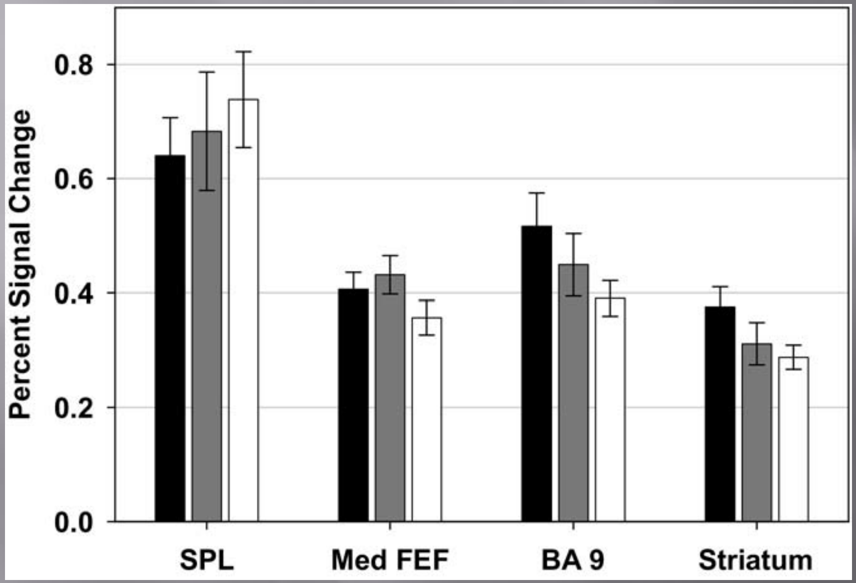
**Table 1.** Average Scores with Standard Deviations on the Four Measures of Task Performance

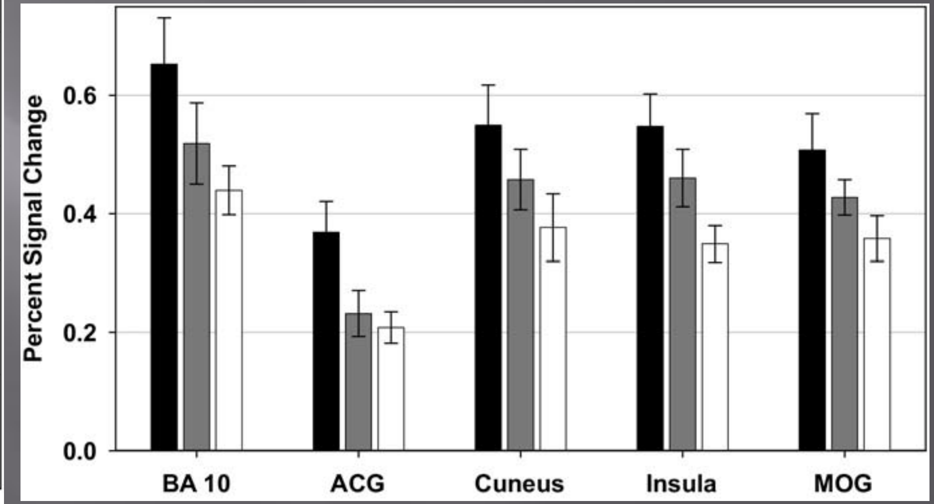
| | Control Subjects ($n$ = 16) | Siblings ($n$ = 16) | Effect Size ($d$) |
|---|---|---|---|
| Latency Prosaccades (ms) | 183.8 ± 30.1 | 205.3 ± 41.4 | .59 |
| Latency Antisaccades (ms) | 251.9 ± 42.9 | 281.0 ± 68.4 | .51 |
| Errors Prosaccades (%) | .5% ± 1.5% | 1.2% ± 2.2% | .37 |
| Errors Antisaccades (%) | 22.8% ± 18.6% | 26.8% ± 21.4% | .2 |




**Raemaekers et al 2005**

# Differences in activation between schizophenia patients relatives and controls for antisaccades and memory saccades




**Camchong et al 2008**

# Quiz

- 1. What is the major difference in visually guided saccade performance between schizophrenia patients and healthy controls?
- 2. What is the major difference in antisaccade performance between schizophrenia patients and healthy controls?
- 3. What is the major difference in memory saccade performance between schizophrenia patients and healthy controls?

# More quiz

- 4. What parameters dissociate antisaccade and memory saccade performance in schizophrenia, affective disorders and obsessive compulsive disorder?
- 5. What parameters of antisaccade and memory saccade performance can be considered as endophenotypes and why?
- 6. What is the neural substrate of the antisaccade and memory saccade deficit in schizophrenia?