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Smooth pursuit deficits in schizophrenia, affective disorder and obsessive–compulsive disorder

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ABSTRACT

Background. In schizophrenia, affective disorders, and obsessive–compulsive disorder (OCD) dysfunction of frontal neuronal circuits has been suggested. Such impairments imply corresponding oculomotor deficits.

Method. Eye movement response to foveofugal and foveopetal step–ramp stimuli was recorded within the same study design in patients with schizophrenia ($N=16$), affective disorder ($N=15$), and OCD ($N=18$) and compared with controls ($N=23$) using infra-red reflection oculography.

Results. In the foveofugal task steady-state velocity was lower in all patient groups compared with controls. Post-saccadic eye velocity was also decreased in patients with schizophrenia and affective disorder. In the foveopetal stimulus steady-state velocity was reduced in schizophrenic patients, only. Changes of saccadic latencies or position errors were not found in any of the patient groups. Also, pursuit latency was unchanged and initial eye acceleration was not decreased.

Conclusions. Unaltered saccadic parameters indicate intact motion perception in cortical visual area V5. Therefore, the observed deficit of pursuit maintenance implies a dysfunction of frontal networks in all patient groups including the pursuit region of the frontal eye field (FEF). In patients with schizophrenia and affective disorder reduced post-saccadic pursuit initiation may indicate an impaired interaction between the pursuit and the saccadic system.

INTRODUCTION

In schizophrenia, affective disorders and obsessive–compulsive disorder (OCD) psychopathological symptoms due to frontal dysfunctions can be observed, such as: loss of inhibitory control over reflexive responses; loss of regulation of social behaviour; changes of affectivity and motivation. Since the oculomotor circuit represents one of the five parallel frontal–subcortical neuronal circuits the integrity of this frontal pathway can be tested by recording of eye movements (Alexander *et al.* 1990; Pierrot-Deseilligny, 1994). The oculomotor circuit includes the frontal eye field (FEF, Brodman area 6 in humans), the supplementary eye field (SEF), the basal ganglia (caudate nucleus, substantia nigra pars reticulata) and superior colliculus, but also receives input from the motion sensitive area in the occipito-parietal-temporal region V5 (MT/MST), the dorsolateral prefrontal cortex (DLPFC) and parietal areas (Brodman areas 7, 39, 40). Two types of eye movements have to be distinguished: (1) saccades to foveate a peripheral target; and (2) smooth pursuit, which is needed to follow slowly moving objects in the environment. Saccades are reflexively triggered by a suddenly appearing visual target and are also under volitional control. With respect to reflexive saccades ambiguous results have been reported for schizophrenia: some authors found prolonged latency and/or reduced spatial accuracy, suggesting a dysfunction within posterior

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parietal areas (Schmid-Burgk *et al.* 1983; Mackert & Flechtner, 1989; Gaymard *et al.* 1998) but others were not able to confirm these results (Fukushima *et al.* 1988; Crawford *et al.* 1998; Karoumi *et al.* 1998). In OCD reflexive saccades were normal, whereas in the antisaccade paradigm error rates were increased in OCD as well as in schizophrenia (Gambini *et al.* 1993; Rosenberg *et al.* 1997; Crawford *et al.* 1998; Karoumi *et al.* 1998; McDowell *et al.* 1999). In this paradigm, reflexive responses towards the target have to be suppressed and a volitional saccade in the opposite direction of the target has to be made. Since the FEF and the DLPFC not only play a major role in control and execution, but also in suppression of reflexive saccades these findings might be regarded as evidence for a dysfunction of frontal areas in both disorders.

A more complex cortical network than the saccadic one is activated during smooth pursuit performance. With a step–ramp stimulus as used in the present study (Rashbass, 1961) one can differentiate between pursuit initiation and pursuit maintenance. The term 'pursuit initiation' refers to the oculomotor response within the first 100 ms of pursuit. In this interval the pursuit movement is only driven by sensory motion information processed in area V5. Visual feedback cannot yet be utilized to optimize eye movement accuracy. In a step–ramp stimulus a target step is followed by a ramp of constant velocity, which can be either foveopetal or foveofugal. In the foveofugal task the elicited saccade and pursuit movement are in the same direction providing information about motion processing. In the foveopetal task target step and velocity ramp are opposite in direction. Thus, the early phase of pursuit initiation before a catch-up saccade is executed can be studied. Information about the ability to maintain smooth pursuit is provided by steady-state eye velocity in both foveofugal and foveopetal step–ramp stimuli. Dysfunction of V5 leads to inaccurate sensory motion processing used by both the saccadic and the pursuit system. Therefore, lesions of area V5 in monkeys not only result in delayed pursuit initiation and reduced eye velocity immediately after the initial saccade in the foveopetal tasks but also in hypometric saccades towards the moving target in foveofugal tasks (Newsome *et al.* 1985; Dursteler *et al.* 1987). Depending on the exact location, lesions of the FEF in monkeys can either affect the saccadic (anterior wall of arcuate sulcus) or the pursuit system (deep in the bank of the arcuate sulcus; Fukushima *et al.* 2002*a*). Lesions of the pursuit region of the human FEF in the depth of the precentral sulcus do not affect the ability to generate correct saccades towards moving targets but impair the integration of motion information to optimize smooth pursuit performance (Heide *et al.* 1996; Rosano *et al.* 2002).

Two hypotheses have been suggested to explain a reduced smooth pursuit velocity and an increased rate of saccades: (1) a dysfunction in frontal areas including the FEF (Levin, 1984; MacAvoy & Bruce, 1995; Sweeney *et al.* 1998); or (2) a motion perception deficit due to a dysfunction of area V5 (Chen *et al.* 1999*a*, *b*). In schizophrenic patients a deficit of pursuit initiation has been demonstrated that was characterized by prolonged pursuit latencies in the foveopetal task and decreased post-saccadic eye velocity in the foveofugal task (Thaker *et al.* 1996; Farber *et al.* 1997; Sweeney *et al.* 1998, 1999). In one study, reduced eye acceleration during pursuit initiation also could be shown (Clementz & McDowell, 1994). Furthermore, decreased steady-state velocities were found giving evidence for a deficit of pursuit maintenance. A deficit of pursuit maintenance together with an excess of mainly catch-up saccades has also been observed during predictive pursuit tasks in schizophrenic patients and their healthy relatives (Holzman *et al.* 1974; Myles-Worsley *et al.* 1991; Arolt *et al.* 1996*a*, 1998; Lencer *et al.* 1999, 2000; Levy *et al.* 2000). There is evidence that this dysfunction is a phenotypic marker for schizophrenia that might be linked to markers on chromosome 6p23–21 (Arolt *et al.* 1996*b*, 1999; Holzman, 2001; Lencer *et al.* 2003). In contrast, latencies and accuracy of saccades elicited by the target step in step–ramp paradigms were normal. This implies that in schizophrenic patients area V5 is unimpaired and that reduced eye velocity during smooth pursuit is due to a dysfunction of the FEF or pathways that result in the inability to use visual feedback, extraretinal and/or predictive mechanisms (Thaker *et al.* 1996, 1999; Sweeney *et al.* 1999). The same pattern has been observed in unmedicated patients with bipolar and unipolar mood

disorder with step–ramp stimuli (Sweeney *et al.* 1999). However, in predictive pursuit tasks, decreased eye velocities together with increased rates of intrusive saccades but not catch-up saccades have been observed implying a deficit different from the impairment in schizophrenic patients (Flechtner *et al.* 1997). To our knowledge, there is only one study in which OCD patients were investigated with a step–ramp stimulus. Oculomotor response was found to be unaltered in a foveopetal task (Farber *et al.* 1997). This is in contrast to those studies that demonstrated a deficit of smooth pursuit maintenance in predictive and non-predictive pursuit ramp tasks (Sweeney *et al.* 1992; Gambini *et al.* 1993; Clementz *et al.* 1996; Pallanti *et al.* 1996). It seems also to be in contrast to the suggested frontal dysfunction in OCD. Thus, several questions remain unanswered.

The aim of the present study was to compare the responses to step–ramp stimuli within one study design between those patient groups (schizophrenia, affective disorder and OCD) in which dysfunctions of frontal neuronal circuits are discussed since findings are ambiguous so far. We used both foveopetal and foveofugal step–ramps to test: (1) whether there is evidence for the hypothesized frontal neuronal dysfunctions in these disorders; and (2) whether distinct patterns of oculomotor performance deficits can be defined for each disorder.

METHOD

Subjects

Patients were recruited by following clinical chart records, whereas controls were recruited by personal contact. Each subject gave written informed consent after having carefully been informed about the study. The study was approved by the local ethic committee. Subjects had to meet the following criteria: (1) stable psychopathological status for at least 1 week; (2) no neurological disease; (3) no significant history of head trauma; (4) normal or corrected to normal vision; (5) no history of substance addiction or CNS-active medication with benzodiazepines or lithium (all of which are known to affect smooth pursuit performance, Levy *et al.* 1993). Operational psychiatric lifetime diagnoses as provided by DSM-IV (American Psychiatric Association, 1994) were established by the German version of the Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan *et al.* 1998). The Structured Clinical Interview for Personality Disorders (SCID-II) (Spitzer & Williams, 1987) was applied to exclude a co-morbidity of a schizophrenia spectrum disorder such as paranoid personality disorder, schizotypy or schizoid personality disorder. Diagnosis had to be agreed upon independently by two experienced psychiatrists (R.L., K.J., or A.K.). To rate symptom severity we used the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962) for all patients. Furthermore, the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) (Goodman *et al.* 1989) was applied in OCD, the Positive and Negative Symptom Scale (PANSS) in schizophrenic patients (Kay *et al.* 1987) and the Montgomery–Åsberg Depression Rating Scale (MADRS) (Montgomery & Åsberg, 1979) as well as the Beck Depression Inventory (BDI) (Beck & Steer, 1998) in patients with affective disorder.

Schizophrenic patients

We included 16 patients with schizophrenia (mean age $32{\cdot}6 \pm 10{\cdot}0$ years; nine male, seven female; BPRS, $34{\cdot}1 \pm 8{\cdot}6$; PANSS, mean positive symptom score $13{\cdot}7 \pm 6{\cdot}3$, mean negative symptom score $19{\cdot}3 \pm 6{\cdot}4$). There were lifetime co-morbidities of abuse of alcohol ($N=1$) and cannabis ($N=1$), but no abuse within 1 year before the study. Nine patients received neuroleptics with a mean daily dosage of 203·4 chlorpromazine equivalents according to Rey *et al.* (1989). Three further patients received a mean daily dose of 5 mg of rispiridone and one patient was on 10 mg olanzapine per day. Three patients were unmedicated for a minimum of 4 weeks.

Major depression

Fifteen patients with episodes of major depression without a co-morbidity of schizophrenia-spectrum-disorder (mean age $41{\cdot}9 \pm 11{\cdot}4$ years; six male, nine female; BPRS, $32{\cdot}2 \pm 7{\cdot}8$; MADRS, $18{\cdot}1 \pm 13{\cdot}2$; BDI, $18{\cdot}4 \pm 10{\cdot}4$) were included. Of these patients 11 were diagnosed as major depressive disorder (single episode or recurrent), four had a bipolar disorder with a major depressive episode at the time of recording. Three patients had had experienced

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psychotic symptoms. There were lifetime comorbidities of: dysthymia (1); social phobia (1); abuse of alcohol (2); post-traumatic stress disorder (1); somatoform disorder (1); and cluster B personality disorders (2). Medication was as follows: four patients with a mean daily dose of 62·5 mg sertraline; three patients with a mean daily dose of 150 mg doxepine; two patients with a mean daily dose of 22·5 mg mirtazapine; one patient with 250 mg amitriptyline/day; one patient with 175 mg trimipramine/day; one patient with 75 mg maprotiline/day; one patient with 225 mg venlafaxine/day; one patient with 20 mg fluoxetine/day.

Obsessive–compulsive disorder

Eighteen patients with OCD (mean age 31·8 ± 8·8 years; 12 male, six female) without any history of psychotic symptoms or schizophrenic-spectrum disorder (BPRS, 37·8 ± 10·7; Y-BOCS, 20·0 ± 7·4). There were lifetime comorbidities of major depression, single episode (1), dysthymia (7), anxiety disorders (4), hypochondria (1), somatoform disorder (1), obsessive–compulsive personality disorder (5), other cluster C personality disorders (5), and cluster B personality disorders (1). Medication was as follows: five patients with a mean daily dose of 120 mg sertraline; three patients with a mean daily dose of 46 mg fluoxetine; two patients with a mean daily dose of 60 mg paroxetine; one patient with a daily dose of 200 mg fluvoxamine; and three patients with a mean daily dose of 175 mg clomipramine.

Healthy controls

Twenty-three healthy controls (mean age 31·5 ± 6·4 years; 15 male, eight female) without any lifetime psychiatric diagnosis were recruited into the study.

Patients with affective disorder were significantly older than schizophrenic and OCD patients as well as controls ($F = 5{\cdot}02$, df = 3, $P = 0{\cdot}003$). BPRS scores did not differ significantly between patient groups indicating same symptom severity in all groups.

Recording and analysis of eye movements

Eye movement recording was performed using a table-mounted infrared reflection oculography device (sampling rate 250 Hz; AMTech GmbH, Weinheim, Germany). The laser spot that served as a target for eliciting smooth pursuit eye movements was projected via a galvanometer onto a white screen. Subjects were seated in 116 cm distance to the screen and with their head immobilized by a chin and a forehead-rest (see also Trillenberg *et al.* 1998).

The non-predictive step–ramp paradigms comprised randomized target steps of 3 ° to the left or the right followed by velocity-ramps of 15 °/s. The ramps were either foveofugal (in direction of the step) or foveopetal (in direction opposite to the target crossing the midline after 200 ms). An interactive computer program developed with MatLab (The MathWorks Inc., Natick, MA, USA) was used to detect saccades and to determine the following parameters.

Foveofugal task (*step and ramp in the same direction*)

For this task, latency and position error (difference of eye and target position, negative values indicate hypometric saccades) of the initial saccade were recorded, this allows conclusions about how precisely the pursuit movement is driven by sensory motion information processed in area V5 to be made. Eye velocity after the initial saccade (averaged in an interval of 50 ms) was measured, to define post-saccadic velocity gain (ratio of eye to target velocity). During this interval of pursuit initiation the eye movement is not controlled by feedback of retinal slip velocity. The interaction between the saccadic and the pursuit system can be studied providing information about V5 and the FEF. Eye velocity in the interval of 500–800 ms after the target step was used to define steady-state velocity gain, which characterizes the ability to maintain the pursuit movement including visual feedback and extraretinal mechanisms such as the integration of the efference copy (posterior parietal cortex, PPC) or prediction (SEF).

Foveopetal task (*step and ramp in opposite direction*)

Since in the foveopetal trial the target crosses midline 200 ms after the step, the reflexive saccade is suppressed and pursuit movement starts immediately. Therefore, the initial saccade generally is a catch-up saccade and pursuit latency is shorter than saccadic latency. We considered (1) latency and (2) position error (see above) of

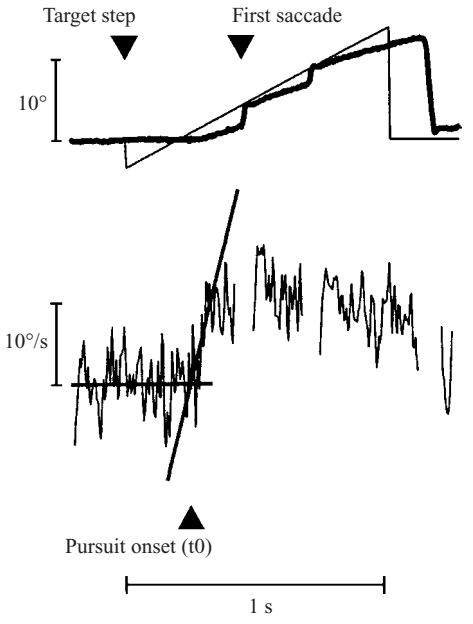

FIG. 1. Example of target and eye position (upper trace) and velocity (lower trace) depicted for the foveopetal task. The first saccade is a catch-up saccade. The slope of the linear fit of eye velocity in a 100 ms interval beginning at t_0 is the initial eye acceleration. The latency of pursuit onset is defined by its intercept with the time (*x*-axis). Eye velocity after the first catch-up saccade was used to define the post-saccadic velocity gain and eye velocity in the interval of 500–800 ms after the target step was calculated to define steady-state velocity gain.

the catch-up saccade. We determined the time t_0 when eye velocity first exceeded three standard deviations of baseline eye velocity. We then fitted a straight line of eye velocity in an 100 ms interval beginning at t_0. The slope of the line is the initial eye acceleration, and its intercept with the time (*x*-axis) defines the latency of pursuit onset (Carl & Gellman, 1987). Both parameters allow conclusions about pursuit initiation and motor function at low eye velocity without feedback (V5 and FEF). For an illustration, see Fig. 1. Furthermore, we determined eye velocity after the first catch-up saccade to define the post-saccadic velocity gain, which reflects the interaction between the saccadic and the pursuit system under feedback control and high eye velocity. Eye velocity in the interval of 500–800 ms after the target step was calculated to define steady-state velocity gain which provides again information about the network including V5, FEF, SEF and PPC.

Statistical analysis

All statistical procedures were performed using the SPSS-PC program (version 10.0). Since age differed between the groups and is known to affect oculomotor performance, we chose an ANCOVA design with age as covariate to test for group effects (Ross *et al*. 1999). Furthermore, pairwise comparisons were performed within the ANCOVA-procedure since no other *post hoc* procedure exists for ANCOVA. The chi-square test was applied to compare percentages between groups.

RESULTS

Foveofugal task

In the foveofugal task we found significant group effects for both post-saccadic velocity gain and steady-state velocity gain (see Table 1). Pairwise comparisons revealed that post-saccadic velocity gain was lower in schizophrenic patients than in controls and OCD patients, and lower in patients with affective disorder than in controls. Steady-state velocity gain was lower in all three patient groups than in controls. This difference was significant for schizophrenic and OCD patients (see Table 1). Comparing post-saccadic velocity gain to steady-state velocity gain revealed that gain increased from the post-saccadic to the steady-state condition in patients with schizophrenia and affective disorder but decreased in OCD patients thus leading to a statistically significant lower fugal gain difference when compared with patients with schizophrenia and affective disorder (see Table 1). Significant group effects were not found either for latency or position error of the initial saccade.

Foveopetal task

We found a significant group effect for steady-state velocity gain, which was significantly lower in schizophrenic patients than in all other groups, as can be seen from Table 2. Furthermore, a significant group effect was observed for initial eye acceleration. This parameter was higher in patients with affective disorder and OCD when compared to controls (see Table 2). However, pursuit initiation prior to the catch-up saccade could be analysed in a lower proportion in the patient groups as compared with

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Table 1. *Comparisons of parameters provided by a foveofugal task between controls, patients with schizophrenia, affective disorder and OCD. Means with standard deviations (S.D.) are shown*

Foveofugal parameter	Controls	Schizophrenia	Affective disorder	OCD	ANCOVA†
Initial saccade					
Latency, s	0·168 (0·036)	0·171 (0·037)	0·177 (0·037)	0·176 (0·039)	NS
Position error, °	−1·22 (0·75)	−1·35 (0·64)	−1·17 (0·52)	−0·82 (0·97)	NS
Velocity gain					
Post-saccadic	0·74 (0·32)[a,c]	0·49 (0·23)[a,b]	0·49 (0·47)[c]	0·73 (0·34)[b]	$F=3·27$*
Steady-state	0·76 (0·16)[d,e]	0·63 (0·22)[d]	0·63 (0·20)	0·60 (0·19)[e]	$F=2·89$*
Gain difference	0·004 (0·33)	0·14 (0·24)[f]	0·13 (0·29)[g]	−0·14 (0·41)[f,g]	NS

† df = 3, 67 in all testing procedures.
Results of pairwise comparisons revealed in ANCOVA: [a] *; [b] *; [c] *; [d] *; [e] **; [f] *; [g] *.
* $P<0·05$; ** $P<0·01$.

Table 2. *Comparisons of parameters provided by a foveopetal task between controls, patients with schizophrenia, affective disorder and OCD. Means with standard deviations (S.D.) are shown*

Foveopetal parameter	Controls	Schizophrenia	Affective disorder	OCD	ANCOVA†
Catch-up saccade					
Latency, s	0·412 (0·097)	0·383 (0·062)	0·433 (0·082)	0·376 (0·074)	NS
Position error, °	0·19 (0·62)	−0·18 (0·42)	−0·21 (0·91)	−0·16 (1·06)	NS
Initial eye acceleration, °/s²	85·98 (23·2)[a,b]	84·73 (27·8)	107·94 (29·60)[a]	109·53 (25·26)[b]	$F=3·68$, df = 3, 44*
Pursuit latency, s	0·155 (0·056)	0·184 (0·040)	0·198 (0·048)	0·177 (0·044)	NS, df = 3, 44
Post-saccadic velocity gain	0·96 (0·20)	0·87 (0·21)	0·88 (0·31)	0·91 (0·32)	NS
Steady-state gain	0·94 (0·1)[c]	0·81 (0·19)[c,d,e]	1·01 (0·1)[d]	0·97 (0·16)[e]	$F=5·87$***

† If not otherwise indicated df = 3, 67.
Results of pairwise comparisons revealed in ANCOVA: [a] *; [b] *; [c] **; [d] ***; [e] **.
* $P<0·05$; ** $P<0·01$; *** $P<0·001$.

controls (11 of 16 schizophrenic patients (69%), nine of 15 patients with affective disorder (60%), nine of 18 patients with OCD (50%), but 20 of 23 controls (87%)). The difference was significant for patients with affective disorder and OCD when compared with controls (affective disorder/OCD/controls, $\chi^2=6·90$, df = 2, $P=0·032$). Thus, increased initial eye acceleration was found in those patient groups with lower fractions of pursuit initiation. Drop-outs included patients who could not suppress the reflexive saccade so that pursuit initiation could not be determined. Significant group effects were not found either for latency or position error of the first catch-up, or for pursuit latency or post-saccadic velocity gain (see Table 2).

DISCUSSION

To our knowledge this is the first study that compares performance in a step–ramp paradigm between patients with schizophrenia, affective disorder and OCD within the same design. Steady-state velocity gain in the foveofugal task was lower in all three patient groups than in controls. In contrast to pursuit initiation, pursuit maintenance is under control of visual feedback. Thus, all three patient groups showed an impairment of pursuit when visual feedback was required. Another reason may be an impaired efference copy signal about the ongoing pursuit eye movement that is a copy of the motor signal generated in the FEF. The efference copy is part of the reference signal that helps to optimize visual perception during eye movements (Haarmeier *et al.* 2001). Taking into account the finding that in all three patient groups reduced pursuit maintenance velocity has been demonstrated in predictive pursuit tasks (e.g. Sweeney *et al.* 1992; Clementz *et al.* 1996; Flechtner *et al.* 1997; Lencer *et al.* 1999; Levy *et al.* 2000) predictive information derived from SEF or FEF might not be integrated, either.

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In none of the patient groups did we find changes of saccadic parameters. Neither latencies nor position errors of the initial saccade in the foveofugal task or the first catch-up saccade in the foveopetal task differed from the control group. This is in accordance with other studies on patients with schizophrenia or affective disorder (Thaker *et al.* 1996; Sweeney *et al.* 1998, 1999). Concerning these parameters, no results have yet been published for patients with OCD. Since the saccadic position error allows conclusions about perceived target velocity this finding suggests that motion perception in the motion sensitive area V5 was intact in all three disorders. Post-saccadic velocity gain after the first catch-up saccade in the foveopetal task did not differ significantly from controls, either, indicating that all three patients groups reached an adequate eye velocity after the first catch-up saccade. In contrast to the initial saccade in the foveofugal task, which was a reflexive saccade (indicated by a latency of about 170 ms), the catch-up saccade in the foveopetal task refixated the target when pursuit velocity was too small. In all patient groups this mechanism of compensation was intact giving further evidence for intact motion perception in Area V5. We found no statistically significant differences of pursuit latencies when compared with controls, and initial eye acceleration was not reduced in patient groups when compared with controls (see also 'Limitations' section). Therefore, we could not find evidence for impaired pursuit initiation in the foveopetal task in our patient groups, which makes a purely frontal motor deficit unlikely.

Since we could not find evidence for a motion perception deficit due to dysfunction in area V5, the observed impairment, of smooth pursuit maintenance points to a dysfunction within frontal neuronal circuits in all three groups including the pursuit region of the FEF deep in the bank of the precentral sulcus. FEF neurons are supposed to create an intermediate representation of tracking eye movements that is distinctly different from those reported in other sensory (e.g. V5) or pure motor areas (e.g. SEF) of the brain (Fukushima *et al.* 2002*b*).

Specific findings in schizophrenic patients

In the group of schizophrenic patients we observed the most severe pursuit impairment, which is line with other studies (Clementz & McDowell, 1994; Thaker *et al.* 1996; Farber *et al.* 1997; Sweeney *et al.* 1998, 1999). Steady-state velocity gain was not only reduced in the foveofugal task but also in the foveopetal task. Although schizophrenic patients did not differ significantly in post-saccadic velocity gain from the other groups on the foveopetal task they could not maintain the gain under steady-state conditions, resulting in low steady-state velocity gain in contrast to patients with OCD and affective disorder. This gives further evidence for impaired integration of visual feedback and extraretinal factors during pursuit maintenance (Thaker *et al.* 1996, 1999). Furthermore, post-saccadic velocity gain in the foveofugal task was also reduced indicating impaired post-saccadic pursuit initiation. This might be due to a dysfunctional interaction between the pursuit and the saccadic system. As mentioned above, we could not demonstrate prolonged pursuit latencies in schizophrenic patients, a finding that has also been reported by Levin and co-workers (1988) who used a search-coil technique, and by Clementz & McDowell (1994). The observed impairments point to a dysfunction of the whole frontal–subcortical network, which might be due to the so-called disconnection syndrome (Friston & Frith, 1995). Evidence for these suggestions might come from imaging studies. In some studies it has been shown that in schizophrenic patients ventricle enlargement was correlated with poor eye tracking (e.g. Blackwood *et al.* 1991), whereas others could not confirm this suggestion (e.g. Katsanis & Iacono, 1991). In relatives of schizophrenic patients who also exhibited eye tracking dysfunction decreased frontal activation in a PET-study was found (O'Driscoll *et al.* 1999). Recently, possible correlates of a disconnection syndrome could be shown by diffusion tensor imaging (DTI) in which white matter abnormalities in schizophrenia were revealed (Foong *et al.* 2000; Agartz *et al.* 2001). Further imaging studies using high resolution techniques like fMRI are needed to reveal the functional and morphological correlates of the smooth pursuit impairment in schizophrenia.

Specific findings in patients with affective disorder

In patients with affective disorder we found post-saccadic gain to be reduced together with

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decreased steady-state velocity gain in the foveofugal task. These results are in line with Sweeney *et al.* (1999). All parameters investigated in the foveopetal tasks were unchanged. The finding of unimpaired steady-state velocity gain in the foveopetal task but impaired steady-state velocity gain in the foveofugal task seems to be inconsistent and is different from the finding in schizophrenic patients. It can be suggested that following the foveofugal task was more difficult than performing the foveopetal task, since gain values in all groups were lower in the foveofugal task when compared to the foveopetal task (see Tables 1 and 2). Therefore, the deficit of pursuit maintenance in patients with affective disorder might become visible only under the more difficult condition. Thus, patients with affective disorder, like patients with schizophrenia, demonstrated impaired post-saccadic pursuit initiation as well as a deficit of smooth pursuit maintenance, which can be explained by a dysfunction of frontal-circuits.

Specific findings in patients with OCD

In patients with OCD we observed significantly lower steady-state velocity gain compared with controls in the foveofugal task, a task that has not been investigated by Farber and co-workers (1997). OCD patients revealed the same decreased steady-state velocity gain as patients with schizophrenia and affective disorder. Therefore, our results support the hypothesis of a pursuit maintenance deficit in OCD (Sweeney *et al.* 1992; Gambini *et al.* 1993; Clementz *et al.* 1996; Pallanti *et al.* 1996) reflecting a dysfunction of frontal–subcortical circuits including the FEF. Like in patients with affective disorder we found parameters of the foveopetal task unchanged (see also Farber *et al.* 1997) and we found no evidence for an impaired pursuit initiation in both step–ramp tasks. Further investigations are needed to define the role of a possible dysfunction of the basal-ganglia in OCD, which might have an influence on oculomotor performance.

Limitations

Due to the naturalistic study design all patients (except three patients with schizophrenia) received psychopharmacological medication. We excluded all patients with CNS-active medication involving lithium or benzodiazepines. Our main results in patients with schizophrenia and affective disorder are in line with those of Sweeney *et al.* 1999, who investigated unmedicated or drug-naïve patients, although we included three patients with rispiridone (see Sweeney *et al.* 1997). Sweeney and co-workers suggested that rispiridone prolongs saccadic latency, decreases saccadic velocity and leads to saccadic hypometria. Since saccadic latencies were normal in all three groups a sedation effect of medication, which would lead to longer reaction times appears improbable. Note, that no significant effect on smooth pursuit performance could be shown for antidepressant medication, in particular, there was no effect of anticholinergic agents on ocular motor variables (Levy *et al.* 1993; Clementz & McDowell, 1994). Therefore, the observed main effects do not seem to be due to medication effects.

The finding of increased initial eye acceleration in OCD and affective disorder is difficult to explain physiologically. One has to take into account that pursuit initiation could only be determined in a smaller fraction of patients compared with controls, a finding that has been also reported by Sweeney *et al.* (1998) for patients with schizophrenia and affective disorder. Therefore, subjects contributing to this result might represent the 'upper end' of 'good performers' within the patient groups, especially patients with affective disorder and OCD. Furthermore, we noted that the noise of the velocity signal was larger in the patient groups compared with controls. This is due to the technical limitations of infra-red oculography and could only be avoided by the use of a search-coil technique. Thus, the beginning of the reference interval for the determination of the initial eye acceleration could have been determined by the noise level and the interval might have been located later in the trace, which may have led to a larger slope of the velocity signal.

Conclusions

In conclusion, we found evidence for a deficit of pursuit maintenance in all three patient groups. This implies insufficient integration of the efference copy of the motor signal in frontal–subcortical networks, including the pursuit region of the FEF. Different patterns and degrees

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of pursuit impairment could be demonstrated: the most severe deficit was observed in schizophrenic patients who showed a pursuit maintenance deficit in both paradigms. Furthermore, we found a deficit in the interaction between the pursuit and the saccadic system if pursuit had to be started after a reflexive saccade in patients with schizophrenia and affective disorder. In patients with OCD no other deficit was observed.

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