Eur Arch Psychiatry Clin Neurosci (2009) 259:483–489
DOI 10.1007/s00406-009-0014-4

ORIGINAL PAPER

Driving simulator performance and psychomotor functions of schizophrenic patients treated with antipsychotics

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Received: 7 October 2008 / Accepted: 8 April 2009 / Published online: 11 July 2009

Abstract The objective of the study is to compare schizophrenic inpatients under antipsychotic monotherapy regarding simulated driving behaviour and psychomotor functions related to driving ability. Schizophrenic inpatients ($n = 80$) were tested before discharge to outpatient treatment. Data were collected with the computerized Act & React Testsystem and the Wiener Testsystem measuring visual perception, reaction time, attention, vigilance and stress-tolerance. Besides, patients underwent various driving simulations on a static driving simulator (FT-SR 200). Before discharge to outpatient treatment, about 25% of schizophrenic patients must be considered as severely impaired with respect to driving skills. Differences between treatment groups could be shown both in psychomotor measures and in driving simulator performance with a better test performance of patients treated with atypical antipsychotics. Controlling for age, psychopathologic symptoms and extrapyramidal signs, differences in psychomotor measures were most pronounced in concentration and vigilance. As mental disorders itself pose an increased risk of accidents, counselling patients with respect to differential effects of antipsychotic treatment is of great relevance. In addition to psychomotor tests computer-simulated driving seems to be a useful tool in assessing traffic safety under pharmacologic treatment.

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Keywords Schizophrenia · Simulated driving performance · Driving ability · Antipsychotics

Introduction

Driving a car is central for the functional autonomy of patients with a psychiatric illness. According to a study of Palmer et al. [1] 43% of middle-aged and elderly schizophrenic outpatients in California are currently drivers. Recent data from a study on mobility behaviour of 1,546 patients in Germany are in line with these results, indicating that about 40% of schizophrenic patients regularly use their cars [2]. From numerous studies it is well known that neurocognitive and psychomotor impairments are key features of schizophrenic disorders that may be present prior to the onset of positive symptoms and persist during periods of remission [3, 4]. Furthermore, it is likely that patients who have difficulties in cognitive and psychomotor functions may have difficulties in coping with social, vocational, or interpersonal demands [5, 6]. There is epidemiological evidence that schizophrenic outpatients may be at a greater risk of motor vehicle accidents per miles driven than age matched controls [7–9]. Clinical data also suggest that there are differential effects of antipsychotic treatment on tasks related to driving skills with an advantage of atypical antipsychotics over conventional neuroleptics [10–14, for a review see 15]. In this context, counselling patients with respect to traffic safety is of great relevance.

Driving a car is a complex, goal-directed activity with different levels of anticipation [16]. Effects of neuroleptic treatment on driving behaviour should be tested both on tasks measuring psychomotor functions and on a level of anticipative control processes like, for example steering,

braking or approaching a risky traffic situation. Because of safety and medicolegal concerns, on road driving tests to determine driving ability under psychoactive drugs are prohibited in most European countries. Computerized simulators offer a useful tool to assess driving skills under pharmacologic treatment in a standardized and safe manner. However, so far there are too few simulator studies to allow conclusions to be drawn about driving safety under antipsychotics [for a review see 17].

Aims of the study

The study was designed to investigate schizophrenic inpatients before discharge to outpatient treatment regarding psychomotor functions related to driving skills and simulated driving behaviour.

Materials and methods

We conducted a comparative clinical study with 80 (49 male, 31 female) inpatients who met the ICD 10 criteria for schizophrenia and who were receiving an antipsychotic monotherapy. The mean age was 32.6 ± 9.8 years (range 18–60 years). Patients were tested under steady-state plasma level conditions before discharge to outpatient treatment. 40 patients were treated with an atypical antipsychotic (20 with amisulpride, 20 with quetiapine), 20 patients received a partial atypical antipsychotic (flupenthixol) and 20 patients were treated with haloperidol. Dosage and choice of medication were selected on an individual clinical basis by the treating psychiatrist. Mean dosages of antipsychotic treatment are given in Table 1.

The study followed a naturalistic nonrandomized design. All participants had a valid driver's licence and gave informed consent. Exclusion criteria were organic brain disorder, substance abuse or mental retardation. All persons gave their informed consent prior to their inclusion in the study. The study was approved by the medical ethics committee of our institution and was conducted in accordance with the Declaration of Helsinki.

Table 1 Mean dosages of antipsychotic treatment

Antipsychotics	Dosage, mg/day[a]	Range
Amisulpride ($n = 20$)	505 (148.8)	200–800
Quetiapine ($n = 20$)	425 (127.0)	300–800
Flupenthixol ($n = 20$)	5.5 (3.1)	3–10
Haloperidol ($n = 20$)	8.8 (5.2)	2–15

[a] Values are shown as mean (SD)

Psychometric measures

On the day of assessment psychopathological symptoms were rated on the brief psychiatric rating scale (BPRS). Furthermore, extrapyramidal signs were assessed with the extrapyramidal symptom scale (EPMS).

Psychomotor tasks

According to the German guidelines for road and traffic safety, data were collected with the computerized Act & React Testsystem (ART 90) and the Wiener Testsystem (WTS) measuring visual perception, reaction time, stress tolerance, concentration and vigilance which were found to be predictive for driving performance in several investigations [18, 19]. These methods have already been described in detail in previous publications [10, 11], and it could be demonstrated that in more than 80% of subjects a correct classification for adjusted and unadjusted driving behaviour could be obtained with results from these test systems.

Visual perception was assessed with the tachistoscope test (TT15), which measures the capability to quickly perceive visual information. The person has to answer multiple-choice questions concerning typical traffic situations that are presented for 0.75 s.

Reactivity and stress tolerance were examined with the reactive stress tolerance test (RST3). Colour, tone and light stimuli are presented in three test phases with 180 signals each. The interstimulus intervals differ within three test phases. In the first trial, stimuli are presented in intervals of 1.58 s, the second phase has an interstimulus interval of 0.95, and in the third phase stimuli appear every 1.07 s. Patients have to press corresponding buttons, bars and pedals with hands and feet.

Concentration was measured with the flexibility and attention test (FAT), where patients have to match simple figures within a defined time. Subjects are asked to decide if the presented figures are identical or different.

The vigilance test (VIGIL) requires the maintenance of attention under monotonous conditions. The movement of a dot within a circular path has to be observed and irregularities have to be identified by a keystroke over a period of 25 min.

Driving simulator

Besides, patients underwent various driving simulations on a static driving simulator (FT-SR 200). The driving simulator used is a static car simulator with videotaped driving scenes that allows researchers to examine responses to traffic situations that cannot be safely evaluated in the field. The driver is seated in a realistic car cockpit with a screen in front of

Table 2 Demographic variables, BPRS and EPMS scores of schizophrenic patients

	Haloperidol ($N = 20$)	Flupenthixol ($N = 20$)	Quetiapine ($N = 20$)	Amisulpride ($N = 20$)	Statistical significance* ($P < 0.05$)
Age, mean (SD), y	41.3 (7.9)	32.5 (10.5)	29.6 (6.1)	27.1 (8.1)	Haloperidol > Flupenthixol Haloperidol > Quetiapine Haloperidol > Amisulpride
Gender (male/female)	13/7	11/9	12/8	11/9	NS
Years of education	11.4 (2.6)	10.4 (1.1)	11.4 (1.5)	10.9 (1.9)	NS
Days since admission, mean (SD)	39.3 (11.7)	38.1 (20.2)	37.3 (13.7)	32.4 (21.8)	NS
Diagnosis[a]					
Paranoid schizophrenia (F20.0)	19	11	10	14	–
Hebephrenic schizophrenia (F20.1)	0	6	3	1	–
Undifferentiated schizophrenia (F20.3)	0	0	5	5	–
Acute polymorphic psychotic disorder with symptoms of schizophrenia (F23.1)	1	3	2	0	–
Brief Psychiatric Rating Scale (BPRS)	53.7 (11.3)	51.7 (10.5)	40.3 (14.7)	40.0 (16.1)	Haloperidol > Quetiapine Haloperidol > Amisulpride Flupenthixol > Quetiapin Flupenthixol > Amisulpride
Extrapyramidal Symptom Scale (EPMS)	0.5 (0.3)	0.4 (0.2)	0.3 (0.3)	0.2 (0.1)	Haloperidol > Amisulpride Haloperidol > Quetiapine Flupenthixol > Amisulpride

NS not significant

[a] ICD 10 Code

him/her. The steering wheel, accelerator and break positions are read by a personal computer. It is possible to display various traffic situations that interact with the driver and to which the driver has to respond. The speedometer and indicator lights in the instrument board also provide feedback. The simulated environment is supplemented by audio effects including engine noise. Four different risk-simulations were presented at a time. Before starting the examination, each driver was familiarized with the simulator by driving a 5-min simulation on a two-lane highway. Afterwards four different risk simulations were presented.

Data analyses

Statistical analyses were performed using SPSS software (Statistical package for Social Sciences, Version 11.5, SPSS Inc., Chicago III, 2002). Demographic and clinical characteristics between groups as well as driving simulator-performance were analysed with nonparametric tests (chi-square and Mann–Whitney *U* test). Product moment correlation between driving simulator performance (percentage of accidents) and psychomotor tests were made using Pearson coefficient correlation.

To test for differences between treatment groups in psychomotor measures, multivariate analyses of variance (MANOVA) were carried out controlling for age, severity of illness and EPMS. Significant simple effects were localized with univariate *F* tests. An alpha value of 0.05 was accepted as nominal level.

Results

As shown in Table 2 treatment groups significantly differed in age, BPRS- and EPMS score (see Table 2). Thus, subsequent statistical analyses of psychomotor functions were conducted controlling for these variables.

Psychomotor measures: global score

In a first step, the overall psychomotor performance was analysed. Corresponding to the German guidelines for road and traffic safety a test has to be considered as failed if a patient falls short of the threshold of 1 standard deviation below mean of normative data derived from a driving-population-representative norm sample. Driving ability is provided if a patient exceeds the threshold in all functional domains investigated. As reported in previous studies [10, 20, 21], we additionally classified patients in "moderate impairment" (i.e. patients failed in less than 40% of test

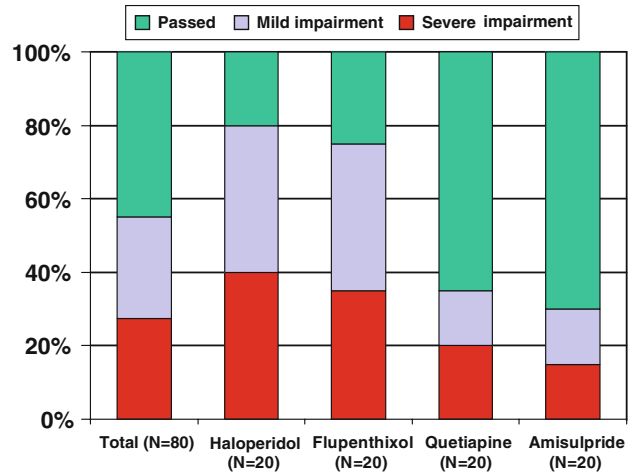

Fig. 1 Global driving ability scores

parameters) and "severe impairment" (i.e. patients failed in more than 40% of test parameters) (see Fig. 1).

Patients who failed to pass the criteria were individually counselled and were informed about legal regulations and consequences.

A percentage of 45 of our sample passed driving ability tests without major impairments. However, in about 25% of the cases, psychomotor performance was considered to be severely impaired, i.e. patients failed in more than 40% of test parameters. There were statistically significant differences between treatment groups, indicating that patients treated with amisulpride or quetiapine showed better results in this global measure when compared to haloperidol or flupenthixol (all $P < 0.01$).

Psychomotor measures: functional domains

Multivariate analysis of covariance (MANCOVA) was performed to assess group differences in psychomotor test variables. Schizophrenic patients treated with haloperidol or flupenthixol significantly differed from patients treated with amisulpride or quetiapine. Main effects of intergroup comparisons in psychomotor measures are given in Table 3.

Univariate F tests were computed in cases in which MANCOVA yielded results at the $P < 0.05$ level.

In the vigilance-task patients treated with amisulpride showed a better performance when compared to patients treated with haloperidol ($F = 9.12$; $P < 0.01$) or flupenthixol ($F = 5.48$; $p < 0.05$). This could also be shown for patients treated with quetiapine when compared to haloperidol ($F = 6.34$; $P < 0.05$).

Patients treated with haloperidol also did worse in the concentration test when compared to amisulpride ($F = 4.98$; $P < 0.05$) or quetiapine ($F = 4.19$; $P < 0.05$).

Driving simulator performance

Results of the driving simulator performance are given in Fig. 2. Analysis revealed a significant better performance in the driving simulation for patients treated with amisulpride when compared to haloperidol ($z = -3.02$; $P < 0.01$) and flupenthixol ($z = -3.08$; $P < 0.01$). This could also be shown for quetiapine-treated patients when compared to haloperidol ($z = -1.92$, $P < 0.05$).

Correlational analyses

To determine relationships between psychomotor tasks and driving simulator performance Pearson correlations were computed. Table 4 lists results of analyses indicating that especially tasks with high demands on psychomotor speed and integration of acoustic and visual stimuli (stress tolerance test–RST3) and the global score showed medium correlations with the driving simulator performance (see Table 4).

Discussion

Patients with schizophrenia could be more liable to accidents because of the disorder itself with cognitive and psychomotor dysfunctions and unwanted adverse effects of antipsychotic treatment. Our patients, derived from a population-representative sample in clinical practice, were examined prior to discharge to outpatient treatment, a clinical situation in which the question "Doctor, when can I drive?" is frequently asked.

The main results of our study were that (1) a great proportion of schizophrenic patients investigated, following psychopathological stabilization and under steady-state pharmacologic conditions, did not pass the threshold criterion according to the German guidelines for road and traffic safety in psychomotor functions, (2) patients treated with atypical neuroleptics (amisulpride, quetiapine) seem to have an advantage with respect to driving skills when compared with patients treated with typical neuroleptics (haloperidol, flupenthixol), and (3) computer-simulated driving seems to be a sensitive tool in assessing driving skills of patients under pharmacologic treatment.

Our results are in line with previous investigations indicating, that about 10–30% of schizophrenic patients considered for discharge to outpatient treatment were severely impaired in psychomotor functions related to driving skills [10–12, 14, 20, 22]. These patients did not reach the criteria of the German road safety board with respect to psychomotor skills in most functional domains investigated, and therefore would be estimated as unfit to drive. Using less conservative criteria, about 15–40% of

Table 3 Performance of schizophrenic patients on psychomotor tests

	Haloperidol ($n = 20$)	Flupenthixol ($n = 20$)	Quetiapine ($n = 20$)	Amisulpride ($n = 20$)	Intergroup comparisons[b]	Analysis	
						F test	*P*
Tachistoscope test (TT15) Correct items	30.8 (3.9)	30.9 (3.8)	33.7 (4.2)	32.7 (3.7)	Haloperidol versus flupenthixol	1.41	NS
Concentration test (FAT) Score[a]	5.4 (4.8)	4.0 (2.0)	3.1 (2.3)	2.6 (1.9)	Haloperidol versus quetiapine	2.72	<0.05
Vigilance test (VIGIL) Score[a]	3.7 (2.5)	3.2 (2.0)	1.8 (0.9)	1.7 (0.9)	Haloperidol versus amisulpride	2.45	<0.05
Stress tolerance (RST3-Phase 1) Omissions	7.5 (6.8)	3.3 (3.2)	2.8 (2.1)	4.1 (7.2)	Flupenthixol versus quetiapine	2.27	NS
Stress tolerance (RST3-Phase 2) Omissions	48.6 (29.1)	42.0 (20.6)	21.7 (21.0)	24.0 (23.3)	Flupenthixol versus amisulpride	2.96	<0.05
Stress tolerance (RST3-Phase 3) Omissions	32.0 (28.0)	21.2 (19.2)	11.4 (10.5)	12.6 (11.2)	Quetiapine versus amisulpride	0.41	NS

Standard deviations in brackets

[a] Reaction time + $\sqrt{}$ [reaction time × (omissions + errors)]

[b] Multivariate analysis of variance with age, BPRS score and EPMS score as covariates

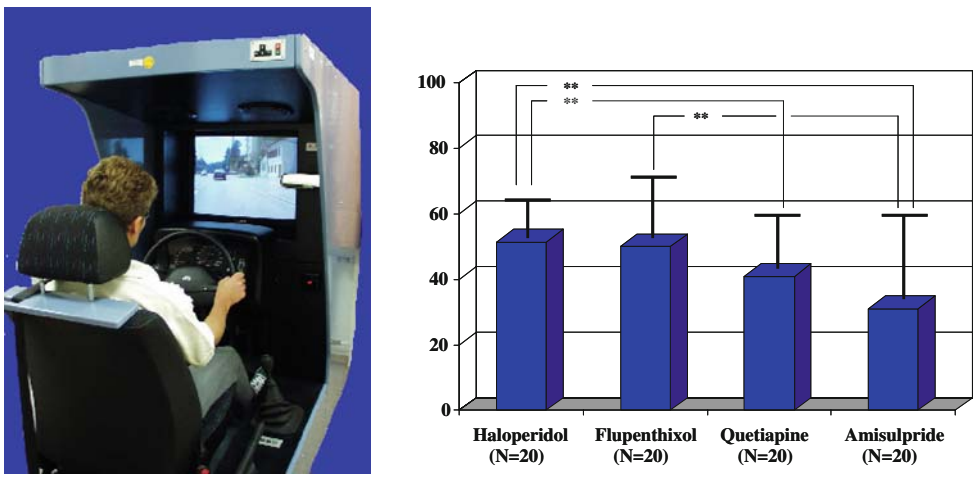

Fig. 2 Driving simulator: percentage of accidents

Table 4 Correlations between psychomotor tasks and driving simulator performance

Psychomotor tasks	Driving simulator performance	
	R	*P*
Tachistoscope test (TT15)	−0.288	<0.01
Concentration test (FAT)	0.409	<0.01
Vigilance test (VIGIL)	0.449	<0.01
Stress tolerance test (RST3-phase 1)	0.507	<0.001
Stress tolerance test (RST3-phase 2)	0.592	<0.001
Stress tolerance test (RST3-phase 3)	0.582	<0.001
Psychomotor performance: global score	−0.678	<0.001

our sample could be classified as "mildly impaired". From a clinical point of view it seems justified to counsel these patients individually, taking into account compensational factors like driving experience, insight in psychomotor dysfunctions and personality traits. 45% of the sample passed all tests without major impairments und could thus be classified as fit to drive.

Before discussing study results, limitations have to be considered. We investigated schizophrenic patients in a clinical routine setting. Causal relationships with respect to treatment effects cannot be drawn within this study design. As patients were not randomly assigned to treatment groups and only patients who were able to participate in a

test procedure that lasted 150 min were enrolled in the study, a selection bias cannot be excluded. All patients were under neuroleptic monotherapy and did not receive any other medication. As polypharmacy is usual in clinical settings, our sample may not be representative. Not least, the external validity of the driving simulator with respect to on the road driving still has to be established.

Patients under atypical antipsychotics seem to show less impairment compared to patients under conventional neuroleptics concerning cognitive performance [23–25]. Within the group of atypical antipsychotics, patients on low 5HT-2A-affinity antipsychotics, such as amisulpride and quetiapine, exhibited a better performance concerning selective attention compared to patients with high 5HT-2A-affinity medication [26]. Amisulpride, both in patients and healthy subjects, had no significant detrimental effects in psychometric tests at lower doses and only mild impairment at higher doses of >400 mg/day [27–29]. Treatment with quetiapine appears to have a positive impact on overall cognitive functions when compared to haloperidol [30], particularly a significant improvement in attentional functions and visuomotor speed under quetiapine was reported [31–34].

The results of our study point to an advantage of patients treated with atypical antipsychotics (amisulpride, quetiapine) in psychomotor functions when compared with typical neuroleptics (haloperidol, flupenthixol). After controlling for confounding effects, a better performance could be shown especially in tasks related to concentration and vigilance. Previous studies on driving ability are in line with these findings indicating that treatment with atypical antipsychotics is more often associated with a better outcome in psychomotor functions [10–12, 14, 20, 22].

Analysis also revealed significant differences in the driving simulator paradigm, which can be associated with anticipative and sensorimotor control processes. It can be speculated, that on this level of performance driving competence becomes more important like, for example accelerating, keeping lane or appraising a risky traffic situation. We could demonstrate significant differences between patients treated with amisulpride or quetiapine, when compared to haloperidol. It is reasonable to assume that also on the level of driving competence there is an advantage of atypical antipsychotics.

The choice between different antipsychotics depends on complex considerations between clinical efficacy and unwanted adverse side effects. For many of our schizophrenic patients, fitness to drive is an important determinant of social functioning and essential for professional conduct. Rehabilitation efforts also have to consider differential effects of pharmacologic treatment on these outcome parameters. From a cognitive point of view driving a car can be regarded as a complex, goal-directed behaviour with different levels of operations. Computer-simulated driving may offer a useful tool to investigate in a safe and reproducible manner effects of psychotropic drugs on different stages of driving behaviour, especially on the level of driving competence. Hence, more patient studies are necessary to determine how different antipsychotics act on different levels of driving performance.

Acknowledgments The authors thank Ms Michaela Wende and Ms Brigitte Peter, medical staff technicians, for administration of the computerized tests and the driving simulator. We also thank Ms Irmgard David for her recommendations on a previous draft of this paper.

Conflict of interest statement There are no financial conflicts of interest to disclose for this study.

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