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ORIGINAL PAPER

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# Fine motor function and neuropsychological deficits in individuals at risk for schizophrenia

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**Abstract** Deficits in fine motor function and neuropsychological performance have been described as risk factors for schizophrenia. In the Basel FEPSY study (**Früh**erkennung von **Psy**chosen; English: Early Detection of Psychosis) individuals at risk for psychosis were identified in a screening procedure (Riecher-Rössler et al. 2005). As a part of the multilevel assessment, 40 individuals at risk for psychosis and 42 healthy controls matched for age, sex and handedness were investigated with a fine motor function test battery and a neuropsychological test battery. Individuals at risk showed lower performances in all subtests of the fine motor function tests, predominantly in dexterity and velocity (wrist/fingers and arm/hand). In the neuropsychological test battery, individuals at risk performed less well compared to healthy controls regarding sustained attention, working memory and perseveration. The combined evaluation of the two test batteries (neuropsychological and fine motor function) separates the two groups into individuals at risk and healthy controls better than each test battery alone. A multilevel approach might therefore be a valuable contribution to detecting beginning schizophrenia.

**Key words** schizophrenia · individuals at risk · fine motor function · neuropsychology

## Introduction

While neuropsychological deficits in schizophrenia have been studied and documented in many studies (Yung et al. 1998), there are not so many studies on fine motor function in schizophrenia, although the latter field has grown recently. However, there are still not so many studies on first episode, let alone neuroleptic naive schizophrenic patients or individuals at risk for schizophrenia regarding this domain. This is surprising, as the investigation of fine motor function could potentially contribute to early detection of schizophrenia.

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## Fine motor function in beginning schizophrenia

### Studies of individuals at risk for psychosis

To our knowledge the investigation of fine motor function began with the pioneering work of Barbara Fish, who in 1987 reported deficits due to neuromotor function impairment and "pandysmaturation" in offspring of patients with schizophrenia. In 1990 Walker and Lewine analyzed home movies showing schizophrenic patients and their healthy siblings during early childhood (up to the age of 5 years). In all, out of 5 schizophrenic patients and their healthy siblings, raters were able to reliably identify patients who later developed schizophrenia by observing the child's behavior and facial expression. This study was the source of further analyses which showed that neuromotor abnormalities and negative facial expression were highly associated with impaired fine and gross motor coordination (Walker et al. 1996). Due to the small sample size, the prognostic validity should, however, be confirmed in further studies. Cannon et al. (1999) investigated 400 children who were diagnosed as having schizophrenia in adulthood and compared them to 408 controls. An unexpected finding of this study was that the children who later developed psychosis had performed just as well as their peers in academic subjects but significantly worse in sports and handicrafts. These findings may indicate that motor abnormalities could be a stable trait marker for being at risk for schizophrenia.

Jones et al. (1994) investigated the associations be-

tween motor development, cognitive and behavioral factors and the development of psychosis in the British birth cohort study. As motor development, particularly the ability to walk, and motor speed were retarded in patients who developed schizophrenia, the authors concluded that retardation in this domain was a risk factor for developing schizophrenia.

McNeil and Cantor-Graae (2000) showed that detecting neuromotor deficits (NMD) could be helpful in identifying individuals at risk for schizophrenia. In their study, 38 % of the healthy siblings of schizophrenic patients had elevated neurological abnormality scores compared to only 5 % in healthy subjects.

### Studies of patients with a first episode of psychosis

Wolff and O'Driscoll (1999) found that approximately one fifth of all neuroleptic-naive first episode schizophrenia patients had increased signs of parkinsonism and pathological neurological soft signs as part of their fine motor function deficits.

Chen et al. (2000) compared 15 Chinese schizophrenic patients with 21 of their nonpsychotic siblings and 26 healthy volunteers using the Cambridge Neurological Inventory. The extent of motor coordination impairment in nonpsychotic siblings was between that of schizophrenic patients and controls. The extent of disinhibition signs was similar in both patients and siblings, but significantly lower in controls. Extrapyramidal and sensory integration signs were the same in nonpsychotic siblings and controls, but significantly more severe in the schizophrenic patients. The authors concluded that motor coordination and disinhibition signs are familial traits, whereas extrapyramidal and sensory integration signs are state-related markers depending on factors such as neuroleptic treatment. Poole et al. (1999) assessed 26 medication-free schizophrenic outpatients and 18 healthy controls. Beside impairment of executive function and inhibition of responses to irrelevant stimuli, the authors found a significant amount of abnormalities in motor coordination in patients with schizophrenia. Furthermore, this impairment of motor function was associated with poor treatment outcome and lower educational advancement. It was also associated with executive deficits and subjects with both deficits performed worst. This leads to the question whether there is a general association of abnormalities in motor coordination with reduced neurocognitive performance.

## Neurocognitive deficits in beginning schizophrenia

### Studies of individuals at risk for psychosis

Cosway et al. (2000) found a significantly worse performance on tests of verbal memory and executive function in young people at high risk for schizophrenia. Jones et al. (2001) detected deficits in sustained and selective attention, and also in executive function in a sample of non psychotic first-degree relatives.

### Studies of patients with a first episode of psychosis

The literature of schizophrenia and neurocognitive function in the field of patients with first episodes of psychosis is extensive. For reviews see Bilder et al. (1991), Hoff et al. (1991), and Riley et al. (2000).

Many studies confirm impairments in neurocognitive and fine motor function in individuals at risk for psychosis and patients with a first episode of psychosis. Several domains, like attention, verbal and visual working memory, and executive function were investigated. But the question of interdependency and of the detection rate of one method alone or in combination is still unsolved. Few of these studies used a combined approach (neurocognitive testing and fine motor function tests) but it is not clear if this combined assessment is useful.

## Aim of the study

In this paper we investigate fine motor function and neurocognitive performance in individuals at risk as compared to healthy controls. It is hypothesized that individuals at risk for schizophrenia performed less well in fine motor function tests and showed impaired neurocognitive performance as compared to healthy controls.

Most studies on fine motor function deficits in patients with schizophrenia and individuals at risk used clinical rating scales. Often, precise quantification and evaluation is omitted. To detect fine motor function deficits we used a computerized and standardized fine motor function test battery.

Different aspects of motor function and neuropsychological performance in individuals at risk and healthy controls are compared. Results from the fine motor function test battery (FMF) and neuropsychological tests in individuals at risk and healthy controls are shown. Furthermore, it is analyzed whether the combination of neuropsychological tests and fine motor function investigation is superior to one battery alone in discriminating individuals at risk from healthy controls.

# Methods

Neuropsychology and fine motor function are investigated as a part of the Basel FEPSY study (**F**rüh**e**rkennung von **Psy**chosen), an early recognition of psychosis project. In the FEPSY study, individuals at risk are identified with a clinical screening procedure, thoroughly examined cross-sectionally on different levels and then followed up over several years.

*Inclusion criteria:* All patients suspected to develop schizophrenia – either referred for that reason to the Psychiatric Outpatient Department of the University of Basel, or detected by the staff of our department – are included consecutively in the screening process and, if appropriate, in the full examination procedure.

*Exclusion criteria:* Severe mental retardation, serious alcohol or

substance abuse (as main diagnosis), serious general illness (potentially) involving organic brain syndrome, age less than 18 years.

Part of the initial examination are tests of fine motor function and neuropsychological performance.

## Study design of the FEPSY study

### Sample description

During the first 36 months of the study we screened 206 individuals, of whom 98 individuals were assigned to the at risk-group (58 agreed to participate in the study). 76 patients were already psychotic at screening. 32 individuals had no risk of psychosis, but other diseases (such as major depressive episode).

From 40 of the above mentioned 58 individuals at risk, data on both fine motor functioning (FMF) and neuropsychological tests were obtained. Of these 40, 20 were women, 20 men, the mean age was 27.4 ± 9.1 years. The control group consisted of 42 healthy individuals without any psychiatric or severe organic disease and without medication (20 women; 22 men; age: 25.9 ± 5.2 years). For distribution of education, handedness, medication and intelligence (verbal, non-verbal) see Table 1. Significant differences between individuals at risk and controls were found in education, verbal intelligence, and nonverbal intelligence but not regarding gender, age and handedness.

Medication of all individuals at risk was documented at the beginning of the study; none of them received neuroleptics. The prescription of low-dose benzodiazepines without daytime sedation was possible.

All participants gave their written informed consent according to the guidelines of the Ethics Committee of the University Hospital Basel, Switzerland.

### Neuropsychological and fine motor function assessment

The neuropsychological and fine motor function assessments were performed by investigators blind to diagnosis and at risk status.

The following instruments were used:

### Assessment of fine motor function

The computerized Fine Motor Function test battery (FMF, "Motorische Leistungsserie Version 3.0" by Schuhfried 1997) was used, with five different subtests: steadiness, precision-steadiness, aiming, tapping, inserting long and short pins. Fine-tuned coordination of the dominant hand was examined by five tests:

- Arm-hand steadiness (holding an electronic stylus inside a "well" 5.8 mm wide, for 20 s without touching the rim),
- Aiming at a target (hitting a row of 20 small points with the stylus),
- Precision-steadiness in line-tracking (negotiating the stylus through a curved passageway without hitting the sides),
- Wrist-finger speed in tapping (tapping the stylus as rapidly as possible on a 40 × 40 mm plate for 20 s),
- Dexterity (inserting long and short pins into holes in a platform).

### Neuropsychological assessment

We used the following neurocognitive test battery to detect cognitive deficits in the areas of intelligence, attention, memory and executive function:

- The Mehrfachwahl-Wortschatz-Test (MWT-A, Lehrl et al. 1990) and the Leistungsprüfsystem, Skala 3 (Horn 1984) are well-validated tests for measuring verbal and nonverbal intelligence.
- The Continuous Performance Test (CPT) measures vigilance in terms of attention, prolonged attention and impulsive behavior (Rosvold et al. 1956).
- The "Testbatterie zur Aufmerksamkeitsprüfung" (TAP) investigates working memory, reaction change and visual scanning (Zimmermann and Fimm 1993).
- The Wisconsin Card Sorting Test (WCST) measures flexibility in thinking, the ability to form abstract concepts and to maintain or change them (Heaton 1981; Drühe-Wienholt and Wienholt 1998).

**Table 1** Socio-demographical characteristics of the sample

| | Individuals at risk | Healthy controls | |
|---|---|---|---|
| Gender (female/male) | 20/20 | 20/22 | $\chi^2 = 0.05$; df = 1 (p = 0.83) |
| Education | | | |
| < 9 | 15 (37.5 %) | 4 (9.5 %) | |
| 9–11 | 13 (32.5 %) | 15 (35.7 %) | $\chi^2 = 15.6$; df = 3 (p = 0.001) |
| 12–14 | 9 (22.5 %) | 23 (54.8 %) | |
| 15–16 | 3 (7.5 %) | 0 (0 %) | |
| Medication (treated/untreated) | 15/25 | 0/42 | $\chi^2 = 19.3$; df = 1 (p < 0.001) |
| Handedness (right/left + ambidexter) | 37/3 | 39/3 | $\chi^2 = 0.04$; df = 1 (p = 0.95) |
| Age (± SD) | 27.4 (± 9.1) | 25.9 (± 5.2) | t = 0.88; df = 61.7 (p = 0.38) |
| Verbal intelligence (IQ) | 105.2 (± 14.4) | 119.0 (± 16.5) | t = 3.6; df = 80 (p = 0.001) |
| Nonverbal intelligence (IQ) | 111.1 (± 10.4) | 118.9 (± 9.5) | t = 4.0; df = 80 (p < 0.001) |

The Tower of Hanoi (ToH) measures the ability of problem solving and planning skills in connection with time-dependent sequential tasks (Gediga and Schöttke 1994).

### Statistical analysis

For statistical analysis we used the Statistical Package for Social Science (SPSS) version 11. All motor functions as well as all neuropsychological domains were evaluated by a computer-based test battery. Due to extreme skewness of the obtained neuropsychological performance measures, we calculated compound measures, the mean z-value of the performance (errors) and the speed of information processing (reaction time). Moreover, compound measures reflect the true capability of a specific cognitive domain in that behavioral strategies are considered (slow and accurate vs. fast and error prone) (Salthouse and Hedden 2002).

If necessary, all variables were transformed by Box-Cox transformation (Box and Cox 1964) in order to obtain normal scores. To increase statistical power, missing data were replaced by regression procedures. This method (Toutenburg et al. 2002) takes into account the complete matrix of covariance. For the sake of stability of variance, a random fraction with a mean of zero and a standard deviation equal to the observed measures was added.

To eliminate potential confounding factors such as medication, verbal and nonverbal intelligence and education, a stepwise regression procedure was performed with the aim to obtain an adjusted and comparable set of data. Due to a complete lack of medication intake by healthy subjects, affected motor and cognitive functions could merely be expected for a small group of individuals at risk. Therefore, intragroup medication effects were eliminated by a sequential sum-of-squares (Type I) analysis (Berres 2004).

Finally, group comparisons and statistical classifications were conducted. This was done by least square t-test and a stepwise discriminant analyses. All stepwise analyses carried out so far used inclusion and exclusion criteria set to 0.05 and 0.1, respectively. Student's t-test results indicated by values $p < 0.05$ were regarded as significant.

## Results

### Results of the fine motor function tests (FMF)

The fine motor function scores of the two groups – individuals at risk for psychosis and healthy controls – were compared. We found significant group differences in three of the five investigated parameters (Table 2), i. e. regarding dexterity as well as velocity of arms/hands and fingers/wrist. Individuals at risk performed significantly worse in these parameters than controls. The most pronounced deficits were found in the two parameters that can be related to the velocity of fine motor function.

### Results of the neuropsychological test battery

In the neuropsychological test battery, we found significant group differences in the compound measures of CPT (missings and false alarms), TAP/Working Memory (missings and false alarms), the WCST (perseveration errors) and TAP/Go/NoGo (missings) (see Table 3). The individuals at risk for schizophrenia performed significantly worse in these tests, showing disinhibition as well as deficits in sustained attention and TAP-working memory. Furthermore, a reduction of cognitive flexibility is indicated by unusually high perseveration errors (WCST).

### Combination of neuropsychological and fine motor function parameters

Discriminant analyses confirmed the results of univariate analyses (Table 3). Covariation with intelligence was taken into account by stepwise logistic regression, which showed that specific motor factors (dexterity and velocity finger/wrist) and neuropsychological parameters (working memory-missings and CTP-false alarm) separate the groups quite well. Using the fine motor function test battery, 69.5 % of the individuals were correctly classified, compared with 70.7 % correct classifications based on the neuropsychological test battery. However, the best results were obtained by using a combination of both test batteries. When combining the motor and the

**Table 2** Comparison of individuals at risk for psychosis and healthy controls: results of the Fine Motor Function Tests (FMF)

| | Individuals at risk (n = 40) Mean (SD) | Controls (n = 42) Mean (SD) | (t; df = 80) Significance |
|---|---|---|---|
| Fine motor function (z-values) | | | |
| Tremor | –0.16 (0.96) | 0.21 (0.95) | 0.37 (p = 0.080) |
| Dexterity | –0.32 (0.91) | 0.45 (0.85) | 4.00 (p < 0.001) |
| Precision | –0.05 (1.02) | 0.17 (0.96) | 1.00 (p = 0.315) |
| Velocity arm/hand | –0.35 (0.97) | 0.28 (0.92) | 3.10 (p = 0.003) |
| Velocity wrist/fingers | –0.39 (1.03) | 0.30 (0.84) | 3.30 (p < 0.001) |

**Table 3** Results of neuropsychological test battery

| | Individuals at risk (N = 40) Mean (SD) | Controls (N = 42) Mean (SD) | (t; df = 80) Significance |
|---|---|---|---|
| Neuropsychology (z-values) | | | |
| CPT (false alarm) | –0.39 (1.01) | 0.38 (0.83) | 3.8 ($p < 0.001$) |
| CPT (missing) | –0.32 (0.94) | 0.34 (0.89) | 3.3 ($p = 0.002$) |
| TAP/Go/NoGo (missing) | –0.38 (0.84) | 0.12 (0.93) | 2.6 ($p = 0.013$) |
| TAP/Go/NoGo (false alarm) | –0.24 (0.93) | 0.13 (1.10) | 1.6 ($p = 0.109$) |
| TAP/Working Memory (missing) | –0.44 (1.06) | 0.39 (0.77) | 4.0 ($p < 0.001$) |
| TAP/Working Memory (false alarm) | –0.34 (0.99) | 0.34 (0.81) | 3.4 ($p = 0.001$) |
| Tower of Hanoi (moves) | –0.05 (1.05) | 0.09 (0.88) | 0.6 ($p = 0.530$) |
| Wisconsin Card Sorting (perseverative errors) | –0.13 (0.99) | 0.31 (0.94) | 2.1 ($p = 0.041$) |
| Wisconsin Card Sorting (perseveration score) | –0.08 (1.01) | 0.23 (0.98) | 1.4 ($p = 0.155$) |

neuropsychological test battery, some of the afore selected parameters were dropped and a core of three parameters (dexterity, velocity finger/wrist and working memory – missings) persisted. This final model classified 74.4 % of the individuals correctly. CPT – false alarm did not contribute to further information anymore. For the combined test battery, we calculated a Wilks Lambda coefficient of 0.70, significant at $p < 0.001$, with a canonical correlation of 0.55 (remaining values see Table 4).

## Discussion

Motor problems handicap individuals in many ways, especially at work. Individuals who have less dexterity and work more slowly are often considered to be less intelligent or even mentally handicapped (Walker et al. 1996). The aim of this part of the FEPSY study was to investigate whether and to what extent a series of simple fine motor tasks and a more complex neuropsychological test battery distinguish a group of individuals suspected to be at risk for schizophrenia from healthy controls. In our sample of individuals at risk, three of five motor factors of the fine motor function test (FMF) showed deficits in fine motor function. Therefore, this test battery might be useful in the detection of individuals at risk for schizophrenia.

It is still an open question to what extent these deficits are a stable marker for beginning schizophrenia. McNeil and Cantor-Graae (2000) studied the stability of specific motor signs during development from infancy to adulthood. The authors found that neuromotor deficits (NMD) can be studied efficiently in infancy, childhood, adolescence and adulthood, but may be unstable over time, especially during the early developmental years. The authors came to the conclusion that a highly standardized investigation method with good interrater reliability is important for the successful investigation of motor deficits in individuals at risk for schizophrenia. For these reasons we used two highly standardized investigation test batteries in our study. These are easy to apply and can be used at varying ages of the tested individuals.

**Table 4** Results of three consecutive discriminant analyses

| | Eigen value | Wilk's Lambda | Canonical Correlation | % correctly classified |
|---|---|---|---|---|
| Neuropsychology | 0.27 | 0.79** | 0.46 | 70.7 |
| Fine motor function | 0.31 | 0.76** | 0.49 | 69.5 |
| Fine motor function and neuropsychology | 0.47 | 0.70** | 0.55 | 74.4 |

** $p < 0.001$

The neuropsychological test battery showed significant differences between individuals at risk for schizophrenia and controls in almost all of the applied tests covering executive function (perseveration errors, CPT false alarm), working memory (working memory and Go/NoGo missings) and vigilance (CPT missings). We also found significant differences in intelligence tests, with lower scores in the individuals at risk.

This can be interpreted in different ways. On the one hand, it might be because of a slowly beginning and developing disease; on the other hand, it may be a premorbid deficit of individuals at risk. The first assumption is supported by the results of the Finnish birth cohort study (Cannon et al. 1999) which found that preschizophrenic children were doing just as well academically as healthy individuals, but had deficits in sports and handicraft. These results imply that the motor abnormalities may be a very early sign of an underlying neurodevelopmental disorder, whereas the neurocognitive deficits might start later.

Concerning the association of motor and neuropsychological deficits, in a prospective study Erlenmeyer-Kimling et al. (2000) found deficits in verbal memory, attention as well as gross motor skills in the offspring of schizophrenic parents. It was possible to correctly identify the offspring of schizophrenic parents who later developed schizophrenia-related psychosis by detecting deficits in verbal memory, gross motor skills and attention. Of the affected offspring, 50 % were detected by combining all three variables. Our results confirm the

study of Erlenmeyer-Kimling in the sense that a combination of both test batteries (neuropsychological tests and the fine motor function test battery) leads to a better identification of individuals at risk, as compared to using a single test battery.

Deficits in executive functions such as a high amount of perseveration errors, working memory impairment and impaired fine motor function in the at risk group might be due to a common underlying pathogenetic mechanism. Maybe this is located in frontal-striatal pathways. Such a mechanism may alter the neurocognitive performance as well as the motor coordination capacity of the affected individuals.

Our findings demonstrate that it is possible to identify deficits in individuals at risk for schizophrenia with a highly standardized test procedure, using the FMF and the neurocognitive test battery at the same point in time in the same individual. The combined discriminant analysis suggests that core motor and neurocognitive deficits can be identified. They are impaired working memory, impaired capabilities and motor velocities in fingers and wrist.

One of the limitations of our study is that we need to wait and see if our "individuals at risk" really develop schizophrenia; four of 20 individuals at risk described here have developed clear-cut psychosis. Also, we need to examine controls with other psychiatric diseases to test the specificity of our findings. Our first preliminary analyses of a control group of first episode schizophrenic patients show the same type of neuropsychological and motor abnormalities, but more severe than in individuals at risk.

We conclude that neuropsychological and fine motor function tests could contribute towards detecting beginning schizophrenia as part of a multilevel approach. The further investigation of these questions is one of our aims in the ongoing Basel FEPSY study.

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