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Intermanual coordination in relation to different clinical subgroups in right-handed patients with schizophrenic and other psychotic disorders

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Abstract *Background* Interhemispheric transfer in psychotic patients is still a controversial issue. Based on the fact that intermanual coordination is associated with interhemispheric transfer, scores in intermanual coordination were investigated in patients with psychotic disorders. *Method* Intermanual coordination was assessed by alternating finger-tapping in 73 adult right-handed in-patients with schizophrenic and other psychotic disorders and was compared with that of 75 healthy right-handed controls. Five clinical subgroups of patients whose diagnoses were based on the DSM-IV classification were specified. *Results* Scores in intermanual coordination in the patients as a whole did not differ from those of the controls. When, however, different clinical subgroups and various manifestations of symptoms were taken into consideration, the scores among those subgroups differed significantly. For instance, patients with residual schizophrenia and chronic symptoms showed lower values in intermanual coordination than did patients with schizoaffective disorders and prevailing acute symptoms. *Conclusions* The assessment of intermanual coordination may provide new insights into the functional coupling of both hemispheres in schizophrenic and other psychotic disorders and may be of a certain prognostic value. Because of its non-invasive, fast and simple application, this approach is thought to be especially suited for investigating acute psychiatric in-patients.

Keywords intermanual coordination · schizophrenic and other psychotic disorders · different clinical subgroups · various manifestations of disorder

Introduction

Motor performances and higher cognitive functions were shown to be closely interrelated. Consequently, motor findings including different finger-tapping test parameters were found to be sensitive indicators of almost all disturbances in the central nervous system. For instance, finger-tapping data changed in relation to mental stress (Murata et al. 1999), hemispheric impairment due to a stroke (Prigatano and Wang 1997), Parkinson's disease (Bronte-Stewart et al. 2000), Alzheimer's disease (Müller et al. 1991) and psychotic disorders (Gorynia et al. 1994). In all experiments using tapping tests, the effects of handedness, gender and age have been taken into consideration (Shimoyama et al. 1990).

As this investigation concentrates on alternating tapping, the relation between alternating tapping and interhemispheric transfer is most relevant for our study. Some investigations point to a relationship between alternating tapping and interhemispheric transfer. For instance, in patients with multiple sclerosis, a correlation was detected between the morphological atrophy of the corpus callosum and the severity of interhemispheric impairment in different functional tasks such as alternating finger-tapping (Pelletier et al. 1993). As a rule, impaired motor transfer was seen to be related to the atrophy of the anterior callosal regions. Moreover, alternating finger-tapping was found to be slower in patients with migraine or patients with multiple sclerosis (MS) and especially in those MS-patients with secondary atrophy of the corpus callosum, which was not the case in the controls (Scherer et al. 1997). In addition to this, studies in patients with callosal agenesis or callosal section showed marked deficits in bimanual performance (Sauerwein and Lassonde 1994), above all, in tasks requiring rapid and alternating movements including finger-tapping (Geffen et al. 1994). Studies, functionally assessing interhemispheric transfer by interhemispheric EEG coherence, showed increased values in children performing only bimanual rhythmic tapping tasks in an

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alternating mode (Knyazewa et al. 1994) and decreased scores in acallosal persons, thus, pointing to a probable relationship between interhemispheric EEG coherence and corpus callosum morphology (Koeda et al. 1995; Knyazewa et al. 1997). Recent data obtained from different finger-tapping tasks focused on learning-related changes, corroborated an association between alternating tapping and interhemispheric transfer which indicated the most pronounced increases in EEG coherence values in the early phase of learning complex tasks in alternating finger-tapping (Andres et al. 1999).

Based on the findings mentioned above, all of which suggest a correlation between interhemispheric transfer and alternating tapping, we want to establish a relationship between the intermanual coordination assessed by alternating tapping and different clinical subgroups of patients with psychotic disorders. The simple application of our patented tapping procedure was thought to be especially suited for acute psychotic in-patients.

Interhemispheric transfer in psychotic patients is still obscure. So far, studies have concentrated on interhemispheric transfer in schizophrenic patients only. Some of them support the idea that disturbances of interhemispheric transfer may be a central problem in schizophrenia (Doty 1989; Randall 1983). In most investigations, the corpus callosum in schizophrenic patients was found to be smaller in size (Woodruff et al. 1995; Tibbo et al. 1998) and only a few studies found either a larger corpus callosum (Bigelow et al. 1983) or no specific change at all in relation to healthy controls (Hauser et al. 1989). Interhemispheric transfer assessed with the help of functional methods showed somewhat increased interhemispheric EEG coherence values in predominantly paranoid patients (Ford et al. 1986) and reduced scores in patients with chronic (Shaw et al. 1983) or negative symptoms (Merrin and Floyd 1996). As a matter of fact, too many differing or even contradicting findings and interpretations must be considered. This may be due to crucial methodological differences (Innocenti 1994; Nunez et al. 1997), but, most of all, to the fact that different groups of patients, often not sufficiently subdivided, were compared. Furthermore, neglecting different manifestations in clinical symptoms as well as the effects of age, gender and handedness may also have contributed to different results.

Hence, the specific aim of the study was to adequately differentiate patients with schizophrenic and other psychotic disorders in terms of their intermanual coordination. In this connection the effects of gender and medication were taken into account. Moreover, the assumption was tested whether patients with chronic manifestation of their disorder performed worse in intermanual coordination than did patients with prevailing acute symptoms.

Methods

Subjects

A total of 73 adult right-handed in-patients (42 males and 31 females) with schizophrenia, schizoaffective and substance-induced psychotic disorders were investigated after giving their informed consent and compared to 75 right-handed controls (34 males and 41 females). The mean age (\pm SD) of the patients was 33.32 (\pm 10.81) while that of the controls was 27.59 (\pm 3.56) years. The patients were clinically evaluated by experienced psychiatrists. The diagnoses of the patients were based on the DSM IV criteria (American Psychiatric Association 2000). Patients with organic brain diseases and those with neurotic as well as somatoform disorders were excluded. All diagnoses were verified by the same psychiatrist. Patients with the following diagnoses were included:

- Substance-induced psychotic disorder (n = 8)
- Paranoid type of schizophrenia (n = 36)
- Undifferentiated type of schizophrenia (n = 7)
- Residual type of schizophrenia (n = 9)
- Schizoaffective disorder, bipolar type (n = 9)
- Schizoaffective disorder, depressive type (n = 4)

According to the main diagnostic features patients were divided into five clinical subgroups:

- Substance-induced psychotic disorder (n = 8)
- Paranoid type of schizophrenia (n = 36)
- Undifferentiated type of schizophrenia (n = 7)
- Residual type of schizophrenia (n = 9)
- Schizoaffective disorder (n = 13)

Clinical symptoms were assessed by a clinical mental status examination using a standardized questionnaire based on the AMDP System (Das AMDP-System 1997), the standard assessment instrument generally applied in German psychiatry. With the help of this questionnaire, clinical symptoms were evaluated. Before we started our investigations, all patients were divided into 3 groups according to the manifestation of symptoms: 1) acute on admission, 2) in partial remission after initial treatment, 3) chronic on admission.

Most of the patients investigated (55 out of 73 patients) had already received anti-psychotic drugs for some time. The remaining 18 non-medicated patients included in this study received no neuroleptic medication prior to their admission to hospital. There was no washout phase.

Procedures

Handedness was assessed by means of the Edinburgh Handedness Questionnaire (Oldfield 1971).

According to the items of the handedness questionnaire, a laterality quotient $LQ = (R-L)/(R+L) \times 100$ was assessed for all subjects. In this study, only right-handed patients with a laterality quotient of 60 to 100 were involved.

After the handedness questionnaire was completed, hand-skill asymmetry was assessed with the help of a tapping-test series.

Tapping-test series

The test was performed from 9:00 to 10:00 a. m. and consisted of five consecutive parts. In sessions one to four, the subjects were required to press a Morse key as fast as possible for a period of 15 seconds under different conditions (with or without concurrent tasks). In these ses-

sions, they were asked to tap first with their right and then with their left index fingers. In part five the subjects were asked to tap alternately with their right and left index fingers, again as fast as possible, for a period of 15 seconds. From the tapping data the following parameter was assessed.

■ Intermanual coordination (IMC)

Intermanual coordination was assessed by alternating tapping. Alternating tapping is a rapid change in right and left finger-tapping which is based on a well-balanced intermanual coordination. While the right finger is pressing the key (i. e. the right finger's motoneurons are excited), the left finger must be relaxed (i. e., the left finger's motoneurons must be inhibited). There are some findings which point to the fact that even during unimanual movements, interhemispheric transfer of information does occur, in order to inhibit the opposite hemisphere, thus, preventing concurrent movements from the other side (Geffen et al. 1994; Tinazzi and Zanette 1998).

To eliminate individual variations in tapping frequency, a mean tapping frequency of both hands was established for each individual subject (mean value of right- and left-hand taps in control sessions 1 and 3 without concurrent tasks) and alternating tapping was related to this mean score. Thus, intermanual coordination was defined as the percent frequency of alternating tapping in relation to the mean tapping frequency of both hands. If the alternating tapping frequency is higher than the mean number of taps in the control sessions, a positive value will be obtained.

$$IMC = \frac{\text{Alternating tapping (right + left)} \times 100}{\text{mean right- and left-hand taps in control sessions (1 + 3)}} - 100$$

This can be illustrated by means of the following example:

Alternating tapping [right-hand taps (39) + left-hand taps (39)] = 78

Mean value of right- and left-hand taps = 69.5 [calculated from control sessions 1 (87/61) and 3 (71/59)]

$$IMC = \frac{78 \times 100}{69.5} - 100 = 12.23$$

The positive value obtained for this person indicates that alternating tapping is 12.23 % above the mean tapping frequency.

■ Statistical analysis

All statistical calculations were based on the SPSS System for Windows, Version 10.0. Due to the fact that in most tests used neither the values of samples were normally distributed nor were equal sample sizes present, non-parametric tests were preferred.

Results

■ Intermanual coordination in relation to gender, medication and different manifestations of disorder

Though non-parametric analysis (Mann-Whitney U-test) for intermanual coordination by gender revealed somewhat higher values for the male patients than for the female ones, this effect was not significant. The same was true of the controls.

Likewise, neuroleptic treatment among the patients was not seen to influence intermanual coordination significantly, i. e., patients with and without medication did not differ markedly in intermanual coordination (Mann-Whitney U-test). Fig.1 clearly shows that in all subgroups non-medicated patients reached approximately the same values in intermanual coordination as did medicated patients, regardless of the type of neuroleptic medication administered at the time of investigation. This figure indicates that it was not the medication but the clinical diagnosis that was decisive for intermanual coordination.

In contrast to gender and medication, different manifestations of psychiatric disorder affected intermanual coordination significantly (Kruskal-Wallis test, $\chi^2 = 18.97$, $df = 2$, $p < 0.001$), cf. Fig. 2. According to the manifestation of their disorder, all patients were divided into 3 groups: (group 1) acute on admission, (group 2) in partial remission after initial treatment, (group 3) chronic on admission. Most patients investigated belonged to group 1 consisting of patients with acute symptoms or to group 2 including those patients with somewhat less acute symptoms due to partial remission who were generally more co-operative. In the chronic

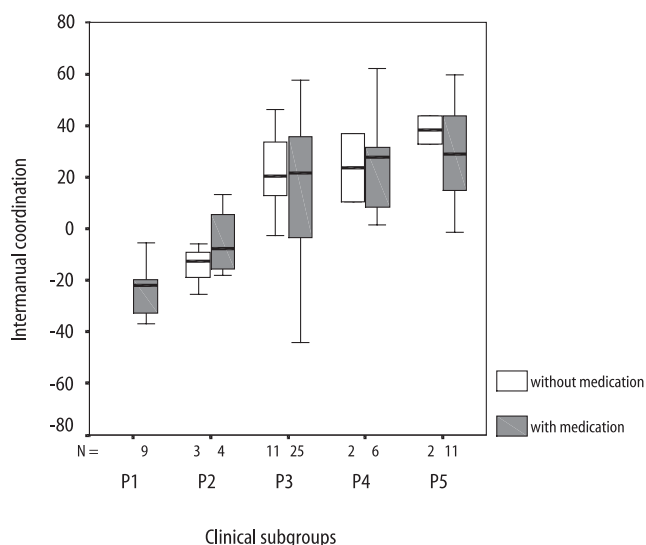


Fig. 1 Boxplots of intermanual coordination in relation to different clinical subgroups without and with medication: residual type of schizophrenia (P1), undifferentiated type of schizophrenia (P2), paranoid type of schizophrenia (P3), substance-induced psychotic disorder (P4) and schizoaffective disorder (P5)

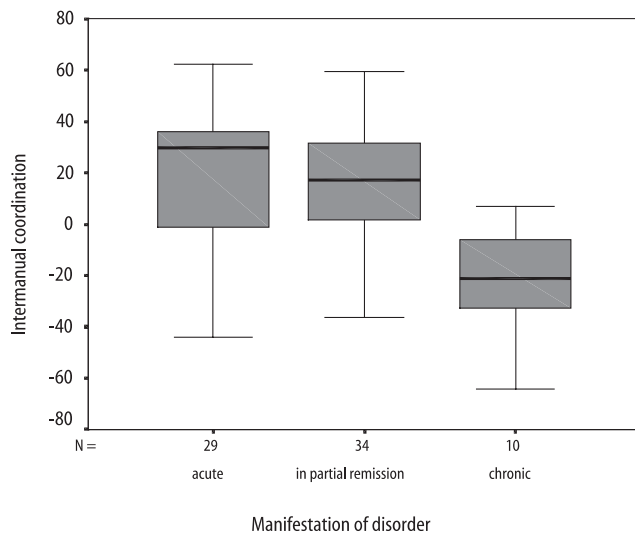


Fig. 2 Boxplots of intermanual coordination in relation to different manifestations of disorder: acute on admission, in partial remission after initial treatment and chronic on admission

group, nine out of ten patients were residual schizophrenics and one patient suffered from an undifferentiated type of schizophrenia. Fig. 2 shows that while the patients with acute manifestation of disorders (group 1) did not differ from those with partial remission (group 2), the patients with chronic disorder (group 3) showed significantly lower scores in intermanual coordination than did the two other groups. Hence, the differences between the chronic patients (group 3) and both patients with acute symptoms (group 1) and less acute symptoms (group 2) were highly significant (for both tests, Mann-Whitney U-test, $p < 0.001$).

■ Intermanual coordination in relation to healthy controls and clinical subgroups

Fig. 3 compares the median values of the healthy controls in intermanual coordination to those of the different clinical subgroups. In this figure, the clinical subgroups were arranged according to their median scores in intermanual coordination, starting with the lowest score of -22.08 in patients suffering from residual schizophrenia (P1) and ending with the highest score of $+32.63$ in patients suffering from schizoaffective disorder (P5).

Without considering diagnostic categories, the median values in intermanual coordination of all the patients and of all the controls investigated were 13.73 and 19.10 , respectively, i. e., all patients performed somewhat worse than did the controls, but this effect was not considered to be of particular significance. According to Fig. 3, however, intermanual coordination in the patients was markedly dependent on clinical diagnosis. Whereas the three subgroups with the highest median values in intermanual coordination (P3 – paranoid schizophrenics, P4 – substance-induced psychotic disorder and P5 –

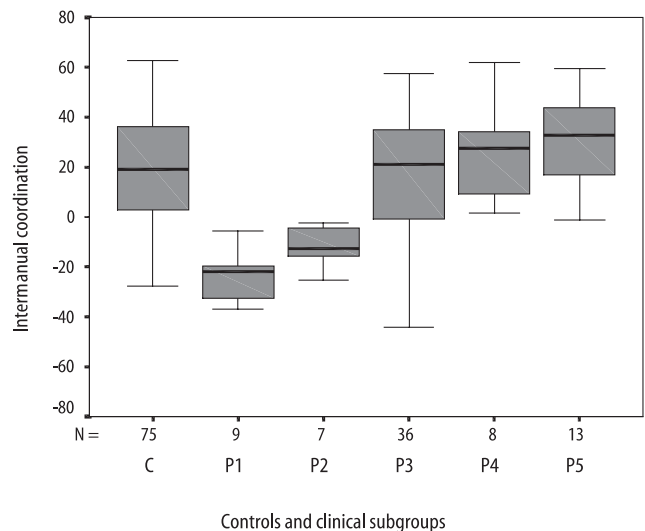


Fig. 3 Boxplots of intermanual coordination in relation to healthy controls (C) and different clinical subgroups: residual type of schizophrenia (P1), undifferentiated type of schizophrenia (P2), paranoid type of schizophrenia (P3), substance-induced psychotic disorder (P4) and schizoaffective disorder (P5)

schizoaffective disorder) did not differ from the controls, the two subgroups with the lowest median values (P1 – residual schizophrenics and P2 – undifferentiated schizophrenics) showed significantly lower values than did the controls. The Mann-Whitney U-test, performed with an alpha correction according to Bonferoni for 5 comparisons ($\alpha/5 = 0.01$) indicated for both comparisons the following value: $p = 0.001$. In addition to this, the comparison of all controls with all schizophrenics (including the residual, undifferentiated and paranoid schizophrenics) revealed significantly lower values in the schizophrenics (Mann-Whitney U-test, $p = 0.013$).

According to Fig. 3, differences were found not only between the controls and the patients, but, above all, between the different clinical subgroups. The Kruskal-Wallis test (for intermanual coordination by five clinical subgroups) revealed a highly significant effect of clinical subgroups on intermanual coordination ($\chi^2 = 29.75$, $df = 4$, $p < 0.001$). The Mann-Whitney U-test, performed with an alpha correction according to Bonferoni for 6 comparisons ($\alpha/6 = 0.008$), indicated that patients with residual schizophrenia (P1) showed significantly lower values in intermanual coordination than did the subgroups P3–P5, i. e., patients with paranoid schizophrenia ($p < 0.001$), substance-induced psychotic disorder ($p = 0.001$) and schizoaffective disorder ($p < 0.001$). In addition to this, undifferentiated schizophrenics (P2) also performed significantly worse than did the subgroups P3–P5, i. e., the paranoid schizophrenics ($p = 0.003$), the patients with substance-induced psychotic disorder ($p = 0.004$) and schizoaffective disorder ($p = 0.001$).

Finally, these analyses made clear that there are significant differences between individual schizophrenic subgroups, as well as between patients suffering from

schizophrenic and other psychotic disorders (schizoaffective disorder and substance-induced psychotic disorder). Furthermore, it is noteworthy that patients with schizoaffective and substance-induced psychotic disorders belong to those subgroups showing the highest values in intermanual coordination and that all patients suffering from substance-induced psychotic disorder used cannabis in combination with other drugs.

Discussion

This study was based on the fact that intermanual coordination is related to interhemispheric transfer. Since interhemispheric communication represents a neurophysiological basis for fundamental cognitive processes (Wong 2000; Christman and Propper 2001; Barry et al. 2002; Ridding et al. 2000), interhemispheric transfer in psychotic patients is thought to be a matter of principal importance (Endrass et al. 2002; Downhill et al. 2000; Meisenzahl et al. 1999; Doty 1989). After testing the effects of gender, medication and manifestation of symptoms on intermanual coordination, the effects of clinical subgroups were related to intermanual coordination. This study revealed that neither gender nor medication influenced intermanual coordination significantly. Our recent study performed among normal subjects (Gorynia and Egenter 2000) also failed to show any obvious effect of gender on intermanual coordination. As far as the effects of medication were concerned, it is worth stressing that although significant differences could be established between the different clinical subgroups, the medicated patients did not differ from the non-medicated patients in any of the subgroups, regardless of the type of neuroleptic medication administered at the time of investigation. The absence of any influence of medication may be due to the fact that in this study the patients were investigated mainly in an acute or sub-acute state of illness. Thus, at that time medication was probably not fully effective. It may be assumed that if the patients had been investigated over the whole course of the disease, the effects of medication would have been visible.

Unlike gender and medication, the different manifestations of psychiatric disorders affected intermanual coordination significantly. Most important was the fact that patients with a chronic manifestation of disorder such as the residual schizophrenics showed markedly lower values in intermanual coordination than did patients of all other groups with a more or less acute manifestation. Individual studies, performed with different methods and carried out among schizophrenic patients were in accordance with our results for the chronic patients. For instance, chronic schizophrenics showed smaller sizes of callosal areas (Stratta et al. 1989) and lower values in interhemispheric EEG coherence (Shaw et al. 1983) than did healthy controls, whereas predominantly acute schizophrenics revealed higher scores in interhemispheric EEG coherence than did healthy controls (Nagase et al. 1992).

The main outcome of this study was the fact that while the healthy controls and the patients as a whole did not differ markedly, different clinical subgroups differed clearly in terms of intermanual coordination. Intermanual coordination ranged from negative scores in patients suffering from residual schizophrenia to marked positive scores in patients suffering from schizoaffective disorder, thus, indicating a strong dependence on clinical subgroups. As expected, patients with residual schizophrenia and chronic symptoms showed lower scores in intermanual coordination than did those patients with schizoaffective disorder as well as substance-induced psychotic disorder and prevailing acute symptoms. In addition to this, not only between schizophrenic and non-schizophrenic subgroups but within schizophrenic subgroups significant differences were also found. For instance, paranoid schizophrenics revealed considerably higher values in intermanual coordination than did the residual and undifferentiated schizophrenics. For that reason, a subdivision of psychotic patients in general as well as of patients with schizophrenic disorders in particular is thought to be most important for intermanual coordination and interhemispheric transfer.

Without considering clinical subgroups in the schizophrenics (including the residual, undifferentiated and paranoid schizophrenics), the median scores in the schizophrenic patients were markedly lower than those found in healthy controls. In line with this finding is the fact that in studies without any differentiation of schizophrenic patients the size of the corpus callosum as an index of interhemispheric transfer was found to be decreased in comparison to healthy controls (Woodruff et al. 1995). While many studies assessing interhemispheric transfer with the help of other methods have not sufficiently taken into account different clinical pictures, for instance different types of schizophrenia or different manifestations of disorder, some studies which undertook a certain subdivision of patients were somewhat compatible with our results. Petsch et al. (1988) and Günther et al. (1989) divided their patients according to the SANS scale into type I schizophrenics with prevailing positive symptoms and short duration of disease and type II schizophrenics with prevailing negative symptoms and long duration of disease. While type I schizophrenics were characterized by an enlarged corpus callosum, type II schizophrenics revealed a smaller corpus callosum.

Furthermore, it is noteworthy that patients with substance-induced psychotic disorder and schizoaffective disorders constitute the two subgroups showing the highest values in intermanual coordination. All patients suffering from substance-induced psychotic disorder developed their psychotic disorder after using cannabis in combination with other drugs. Hence, cannabis abuse may be a risk factor for schizophrenia (Baigent et al. 1995; Bersani et al. 2002) and may be associated with higher values in intermanual coordination. For the time being, there are only a few studies supporting the idea of

a higher interhemispheric transfer in cannabis abuse. For instance, daily cannabis users in contrast to non-users indicated increased interhemispheric coherence values of theta activity in frontal areas. This was established in both psychiatric patients (Struve et al. 1994) and normal subjects (Struve et al. 1999). The effects of cannabis will have to be validated in further experiments.

Finally, it may be noted that among all psychotic patients, the residual schizophrenics with the lowest values in intermanual coordination were characterized by chronic manifestation of the disorder, predominantly negative symptoms as well as worse clinical prognosis, while patients with schizoaffective disorder with the highest values in intermanual coordination were marked by more or less acute, predominantly positive symptoms and better clinical prognosis. It may be assumed that psychotic patients with higher values in intermanual coordination which did not decisively differ from those of the controls (in this study patients suffering from paranoid schizophrenia, substance-induced psychotic disorder and schizoaffective disorder) may be associated with more favorable clinical findings. Thus, a better intermanual coordination, i.e., a better interhemispheric communication is thought to be an advantageous condition in psychotic patients. This idea needs to be proved in further experiments.

Conclusions

This study has shown that the assessment of intermanual coordination may provide new insights into the functional coupling of both hemispheres in psychotic disorders and may be of a certain prognostic value. Because of its non-invasive, fast and simple application, this approach is especially suited for investigating acute psychiatric in-patients.

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