Neurological soft signs in Twins discordant for Schizophrenia

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Introduction

In contrast to "hard signs" which can be localized to specific brain regions and typically involve motor or perceptual systems, unspecific minor sensory and motor neurological abnormalities are summarized as neurological soft signs (NSS). NSS have been reported to be more common among schizophrenic patients than among various control groups and are not dependent on neuroleptic medication [1, 2]. The rate of NSS was found to be high in siblings of schizophrenic patients [3]. Moreover, two twin studies with 15 [4] and 13 [5] twin pairs discordant for schizophrenia found more NSS in non-affected discordant twins than in controls, suggesting that NSS are at least in part genetically determined.

The aim of this study was to investigate whether NSS and more specifically laterality phenomena of the NSS are under genetic control in schizophrenia. Therefore, we examined NSS in identical healthy twins and twins discordant for schizophrenia.

Subjects and Methods

The study group consisted of 30 monozygotic twins: 13 pairs discordant for schizophrenia (10) or schizoaffective psychosis (3) and 17 healthy control pairs. The groups did not differ in regard of age, sex, and education. (see Table 1 for detailed soziodemographic information).

The NSS were examined blindly to diagnosis according to the Heidelberg Manual (see Table 2), which consists of 16 items. Eleven of these items were scored for each body-half separately.

	Controls	Non-affected discordant	Affected discordant
n	34	13	13
Sex (f/m)	7 / 17	5 / 13	5 / 13
Age	31.1 (9.0)	31.5 (10.1)	31.5 (10.1)
Years of school	11.2 (2.0)	10.9 (1.8)	10.5 (1.6)
BPRS-Score	-	-	29.6 (7.3)
CPE (mg/kg)	-	-	140 (237)

Table 1:
Soziodemographic data of healthy control twins, non-affected twins of discordant pairs, and affected twins

Statistical Analysis

Since twins are not independent, statistical analyses were performed not on single subjects but on twin pairs using a repeated measures design. A within pair variable "member" was created with affected vs. non-affected discordant twins. Each twin of each control pair was randomly assigned to one of two groups (comparison group A vs. B). Three two-way analyses of variance (ANOVA) with total-NSS-scores, motoric-NSS-scores, and sensoric-NSS-scores as dependent variables were calculated. To assess hemispheric differences a three-way ANOVA was calculated with group as independent variable, member and body-half (left vs. right) as between pair factors. All post-hoc analyses were performed by Newman-Keuls Test.

Table 2: ***Heidelberg Manual***

Ozeretzki´s test
diadochokinesis
pronation/supination
finger to thumb opposition
speech articulation
station and gait
tandem walking
2 point discrimination
finger to nose test
fist-edge-palm test
right/left orientation
face/hand sensory test
graphesthesia
stereognosis
mirror movements
arm holding test

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Results

The two way ANOVA for NSS-total-score yielded a significant group vs. member interaction ($F(1/28)=6.0$; $p=.02$). Affected twins (10.6±6) as well as non-affected twins (8.0±5.2) of discordant pairs showed significantly higher total NSS-score than controls. Additionally, NSS-total-score was higher in the affected compared to the non-affected twins of discordant pairs whereas control twins were not different from each other (4,2±1,8 resp. 4,8±2,4) (Fig.1). Similar group differences appeared, when only motor items were included (group x member interaction $F(1/28)=6.4$; $p=.02$). Post-hoc analyses showed significantly higher motor NSS-scores in affected (7.3±3.4) and in non-affected (5.3±4) discordant twins compared to controls (3.0±1.5 resp. 3.4±2.0). Affected twins of discordant pairs scored significantly higher than their non-affected co-twins (Fig.1). With respect to sensory items no significant effects were revealed.

The three-way ANOVA showed a nearly significant group x body-half interaction ($F(1/28)=3.1$; $p=.08$) due to nearly significant ($p= .08$) higher NSS-scores on the left than on the right body half only in discordant twins (Fig. 1). The group x body-half x member interaction was not significant ($F(1/28)=1.5$; $p= .2$).

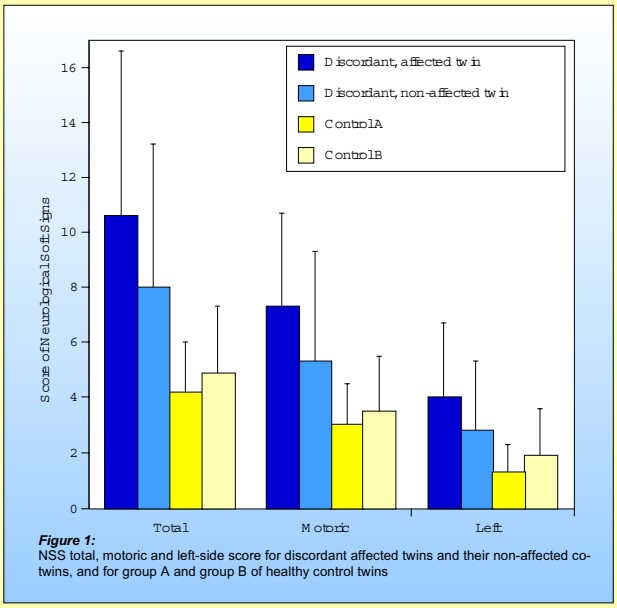

Figure 1:
NSS total, motoric and left-side score for discordant affected twins and their non-affected co-twins, and for group A and group B of healthy control twins

Discussion

Two major findings emerged in this study: first, higher NSS-scores were recorded in affected and non-affected twins of discordant pairs than in healthy twins. This confirms that NSS occur more frequently in schizophrenic patients than in healthy controls. Our finding that non-affected twins of discordant pairs did differ in their NSS-scores suggests a genetic contribution, as the non-affected twins have the same genotype, but never showed schizophrenic symptoms. In this respect, our findings corroborate the NIMH twin studies. Taking into account that affected twins of discordant pairs show higher NSS than their co-twins, our results suggest that genetics may determine a set point for NSS around which dynamic state fluctuations may occur.

Second, both, affected and non-affected twins of discordant pairs, showed a *trend to* higher NSS-scores on the left than on the right body-half. In contrast, Torrey reported a lateralization of NSS to the right body-half suggesting a left-hemispheric dysfunction [6]. However, he had investigated only sensory functions (graphesthesia, face-hand test), whereas our scale predominantly includes motor phenomena. Indeed, a detailed analysis showed that our findings are due to motor dysfunctions lateralized to the left body-half.

Thus, our findings are in line with an increasing number of reports suggesting that the notion of an isolated left-hemispheric dysfunction in schizophrenia might be a simplification. In contrast, in more recent concepts schizophrenia is conceptualized as a disturbance of distributed brain circuits. Our findings indicate that the disturbance of these fundamental integrative functions is genetically transmitted.

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