Eur Arch Psychiatry Clin Neurosci (2001) 251 : 18 – 23

ORIGINAL PAPER

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Effects of cerebral hemispheric laterality on the span of apprehension of schizophrenic and healthy subjects

Received: 31 May 2000 / Accepted: 17 October 2000

Abstract The effects of hemispheric laterality on a forced-choice Span of Apprehension (SoA) task were investigated. Forty-eight adult schizophrenic inpatients were recruited. A control group of healthy subjects was put together using the matched-pairs method with age, gender, and education as control variables. SoA performance was determined separately for the left and right visual field (VF), respectively. No SoA group differences were found; in both groups, the hit percentage was higher in the right VF. However, in the schizophrenic group, the left VF performance showed significant negative correlations with psychopathologic symptoms (especially auditory verbal hallucinations). In a subsample of patients receiving atypical neuroleptic drugs, the daily dosage correlated negatively with left VF performance. In general, young subjects performed better than old subjects (both VFs), males performed better than females, and subjects with high education performed better than subjects with low education (right VF).

Key words Span of apprehension · Schizophrenia · Cerebral hemispheric laterality · Psychopathology

Introduction

The forced-choice Span of Apprehension (SoA) task (Estes and Taylor 1964) is a prominent paradigm in neuropsychological research on attention and information processing of schizophrenics. Neale et al. (1969) and Neale (1971) showed siginificant SoA impairments of schizophrenics compared to other clinical and non-clinical groups; however, Strauss et al. (1984, 1987) failed to discriminate schizophrenic from manic patients. Asarnow et al. (1977) found SoA deficits in foster children of schizophrenic biological mothers. Remitted schizophrenic groups were also discriminated from controls in a SoA task (Asarnow and MacCrimmon 1978, 1981). SoA is related to negative symptoms (Nuechterlein et al. 1986; Hain et al. 1993; Strauss et al. 1993) and to the deficit syndrome of schizophrenia (Buchanan et al. 1997). It has been assumed (Asarnow et al. 1991) that SoA tasks tap several cognitive processes: decay of iconic and working memory, transfer from iconic to working memory, and the serial/parallel scan processes with which the contents of the iconic and/or working memory are detected. Deficits in SoA performance are considered markers of cognitive vulnerability to schizophrenia (Nuechterlein and Dawson 1984; Nuechterlein et al. 1986; Asarnow and Granholm 1991; Nuechterlein et al. 1991).

There is a substantial and growing body of literature on intra- and interhemispheric information processing in schizophrenia (for a review see Walker and McGuire 1982). Most of the localizationist research has evolved around hypotheses of left-hemispheric dysfunctions (e. g., Flor-Henry 1969; see also Gruzelier 1991). Other authors (Venables 1984; Oepen et al. 1987; Cromwell 1987; Cutting 1994) suppose a primary, pathogenetic right-hemispheric impairment of attentional functions which cause the deficit in higher left-hemispheric processes of schizophrenia. The first author who linked auditory verbal hallucinations (AVH) with the right cerebral hemisphere was Jaynes (1979) with the speculative but fascinating theory of the "bicameral mind". Cutting (1990) lined out the theory that AVH in schizophrenics may result from an underactivity of the right hemisphere. He suggested that verbal thoughts, presumably arising from the left hemisphere, lack their "… accustomed tone […] which stamps them as uniquely

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ours [...] because of the loss of the right hemispere's prosodic contribution" (Cutting 1990, p 264). David (1994) proposed scientific proofs which would support this theory, e. g., excess of AVH in left-handed schizophrenics or female patients. Indeed, Tyler et al. (1995) reported a relationship between AHV and left-handedness, while Bardenstein and McGlashan (1990) found more AVH in female schizophrenics.

The technique of lateral tachistoscopic stimulus presentation is one of the most important sources of information for the study of functional asymmetry of the brain hemispheres (e. g., Posner et al. 1988; Strauss et al. 1992). The rationale of this method is based on the anatomical property of the visual system whereby stimuli presented in one lateral visual field are transmitted along neural pathways to the contralateral brain hemisphere. Effects of hemispheric asymmetry on the visual SoA performance have rarely been examined. Elkins et al. (1992) investigated the relationship between brain laterality and SoA performance in schizophrenics, depressives and normal controls. They found that stimuli displayed in the left visual field were performed more poorly by all groups, but schizophrenics were especially impaired, thus confirming the hypothesis of a right-hemispheric attentional deficit of schizophrenia; relations between SoA performance and schizophrenic psychopathology were not investigated. To our knowledge this is the only examination of laterality effects on the SoA.

Therefore, the main aim of the present analyses is the further investigation of the effects of hemispheric laterality on a forced choice SoA task in schizophrenics and healthy controls. The relationship between lateralized SoA performance and schizophrenic psychopathology, especially AVH, will be examined; furthermore, relations with antipsychotic medication and sociodemographic core variables will be investigated.[1]

Methods

Subjects

Forty-eight adult inpatients with a diagnosis of schizophrenia were recruited from the Northern Clinic, Hamburg-Ochsenzoll, and from the University Hospital, Hamburg-Eppendorf. Thirty-eight patients (79.2 %) fulfilled the ICD-10 (World Health Organization 1992) criteria of paranoid schizophrenia (code F20.0), three patients (6.3 %) were of the hebephrenic type (F20.1), and seven patients (14.6 %) were of the residual type (F20.5). Diagnostic criteria according to ICD-10 were checked with the International Diagnosis Check Lists (IDCL; Hiller et al. 1995). Seventeen of the schizophrenic patients were on typical neuroleptic (NL) treatment (mean of daily dosage in equivalence to chlorpromazine: 278 mg); 26 patients took atypical NL (equivalence mean: 236 mg). Three patients received both typical and atypical NL (equivalence mean: 216 mg), and two patients received no NL at all. Additionally, 16 patients received benzodiazepines (median of dosage in equivalence to lorazepam: 2.2 mg), and 11 patients received other medication (e. g., biperidene, antidepressants). Calculation of NL equivalents were based upon algorithms by Jahn and Mussgay (1989). A control group of healthy subjects was composed using the matched-pairs method with age, gender, and educational level as control variables (see Table 1).

Tab. 1 Characteristics of the schizophrenic and the control sample

	Schizophrenics (N=48)	Controls (N=48)
Age[1], mean (SD)	34.5 (10.1)	35.0 (10.9)
Gender	31 males, 17 females	31 males, 17 females
Educational level	8 elementary school 16 middle school 24 high school[2]	8 elementary school 16 middle school 24 high school[2]
Age at first admission[1], mean (SD)	30.5 (8.4)	–
Duration of illness[1], mean (SD)	4.0 (6.0)	–
No. of admissions, mean (SD)	4.3 (6.7)	–

[1] Years, [2] Qualifying for entrance to university

All participants were right-handed, free of alcohol or drug consumption, organic brain disorder, severe somatic disorder, and had normal or corrected-to-normal vision.

Materials and procedures

A computerized forced-choice SoA procedure (Wagner et al. 1992) was presented on an IBM compatible PC with a 3/86 microprocessor and a CPA 425 LR monitor. In a randomized order, either 3 (16 stimuli) or 8 (80 stimuli) consonant letters falling in a 4 × 4 matrix were displayed (presentation time: 100 ms). Every display contained either the letter "F" or the letter "T", but never both. The 2 or 7 distractor letters were chosen randomly from the remaining consonants of the alphabet. An example for a SoA stimulus (8-letter condition) is given in Fig. 1

The patients were instructed to press the left cursor key when detecting "F", the right cursor key when detecting "T", and to guess (right or left cursor key) when in doubt. Target and noise letters were equivalently distributed across the cells of the 4 × 4 matrix. The visual angle of the display was about 15° × 15°. Each subject was seated 65 cm from the monitor. The total test duration was about 8 min. The SoA performance measure was the percentage of correct reactions during the 8-letter condition (the 3-letter condition served only as a general motivational control).

Immediately before every stimulus presentation a small white spot appeared in the center of the array; the subjects were instructed to fix this point throughout the test. The brief target exposure time (100 ms) precluded saccadic eye movements. Therefore, any effect which is restricted to the right or left visual field, respectively, can be related primarily to the left or right brain hemisphere, respectively.

For analyses of hemispheric performance, the 4 × 4 matrix was subdivided into the left, central, and right visual field (VF; see Fig. 2). Since the central visual field was defined to investigate differences between central and peripheric SoA which are not of interest for the present analyses, the SoA performance was considered only for the left and right VF, respectively.

Fig. 1 Example for a stimuli of the SoA task (8-letter condition)

1 Another part of this study which refers to Continuous Performance Test data obtained from the same sample has already been published in Mass et al. (2000).

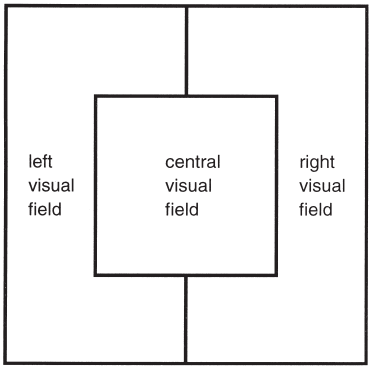

Fig. 2 Subdivision of the SoA 4 × 4 matrix in a left, a central, and a right visual field (only the left and right visual field, respectivlely, are considered in the present analyses)

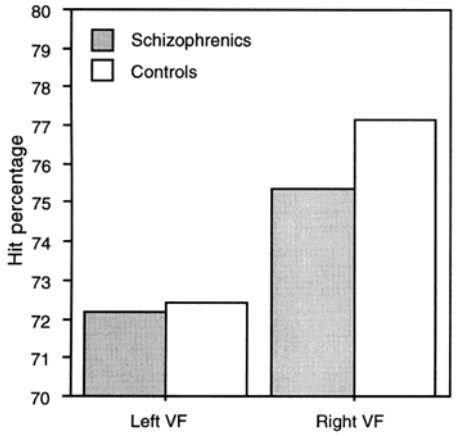

Fig. 3 SoA performance of schizophrenics and controls (8-letter condition)

Psychopathology of the patients was assessed by the authors. After a semistandardized interview symptoms were rated using the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987). Only the seven positive (e. g., delusions, hallucinatory behavior) and the seven negative symptom ratings (e. g., blunted affect, emotional withdrawal) were considered in this study. Due to the detailed definitions of the seven different levels of symptom severity, Bell et al. (1992) reported good-to-excellent interrater reliabilities for most of the PANSS items.

All subjects filled out the Eppendorf Schizophrenia Inventory (ESI). This is a clinical questionnaire for the measurement of characteristic subjective experiences of schizophrenia. Since this instrument is a new development, a short description will be given in the following (for detail see Mass 2000, in press). The ESI includes four subscales: (1) "Attention and Speech Impairment" (AS, ten items), describing impairments of the adequate reception and interpretation of environmental stimuli, above all affecting speech. Typical statements of this subscale are: "If someone speaks to me, I often can't grasp the meaning of the words correctly." or "When I watch television, it is difficult for me to follow the pictures and words and to catch the story simultaneously." (2) "Ideas of Reference" (IR, seven items), representing a tendency to interpret trivial events in an excessive meaningful way and a delusional mood; typical statements are: "Now and then events, broadcasts etc. seem to be related to me although it is actually impossible." or "Sometimes I think that certain signs are given personally to me which no one else can observe." (3) "Auditory Uncertainty" (AU, eight items); it describes an insecurity to discriminate between thoughts and words which actually have been heard and, furthermore, a vague impression of being influenced is part of this scale. Typical statements: "Even if I hear something very clear sometimes I am not sure whether I just imagined it." or "Sometimes I hear my 'inner voice' as distinctly as if someone actually is talking to me." (4) "Deviant Perception" (DP, nine items) refers to aberrations of perceptual processes, especially involving disturbances of the body-image. Typical statements: "Sometimes a part of my body seems to be smaller than it really is." or "Now and then I dont feel my limbs properly when I move."

The reliability coefficients (Cronbach α) of these subscales obtained from a sample of 239 schizophrenic inpatients are 0.87 (AS), 0.85 (IR), 0.79 (AU), and 0.82 (DP), respectively. The validity of the ESI has been shown by significant correlations between the four subscales and psychopathological, neuropsychological, and questionnaire data (see Mass 2000).

The statistical analyses were conducted with the Statistical Package for the Social Sciences (SPSS), Release 6.1.1 for Macintosh. All significances are two-tailed.

Results

The schizophrenic group reached a mean (SD) hit percentage of 72.2 (10.5) for the left VF, and 75.4 (11.8) for the right VF. The corresponding results of the control group were 72.4 (11.2) for the left VF, and 77.1 (10.4) for the right VF.

A 2 (groups) × 2 (visual fields) ANOVA yielded no significant group effect ($F[1, 94] = 0.34$, n. s.), a significant VF effect ($F[1, 94] = 8.01$, $p < 0.01$), and no significant group × VF interaction effect ($F[1, 94] = 0.28$, n. s.). In both groups, the hit percentage was higher in the right VF (see Fig. 3).

To evaluate the relationship between SoA performance and schizophrenic psychopathology, correlations were calculated between the two VF hit percentages on the one hand and the positive or negative PANSS items and the ESI scales on the other hand (see Table 2). Only SoA performance in the left VF showed significant negative correlations with the following psychopathological variables: the PANSS item "Hallucinatory Behavior" and the ESI subscales "Attention and Speech Impairment", "Auditory Uncertainty", and "Deviant Perception".

The relationship between antipsychotic medication and SoA is shown in Table 3. Across all patients, the total neuroleptic dose correlated with SoA performance in the left and right VF, respectively: a high dose was related to poor performance and vice versa. However, when distinguishing between typical (mostly Haloperidol) and atypical NL, the atypical NL dose (mostly Clozapine) correlated negatively with left VF performance.

To examine the meaning of sociodemographic core variables on SoA performance, multiple stepwise regression analyses were calculated for each of the two VFs with age, gender, and school education as independent variables. Age predicted SoA performance in both VFs (left VF: Beta = – 0.33, $p < 0.001$; right VF: Beta = – 0.36, $p < 0.001$). In addition, right VF performance was predicted by gender (Beta = – 0.23, $p < 0.01$) and educational level (Beta = 0.34, $p < 0.001$).

Tab. 2 Means and SDs of PANSS ratings and ESI subscales; correlations (PANSS: Rho; ESI: r_{xy}) with SoA performance (schizophrenic sample)

	Descriptives		Correlations with SoA	
	Mean	SD	Left VF	Right VF
P1, Delusions	2.69	1.37	– 0.13	0.10
P2, Conceptual Disorganisation	2.73	1.12	– 0.10	0.07
P3, Hallucinatory Behavior	1.96	1.30	– 0.37**	0.07
P4, Excitement	1.48	0.87	– 0.05	0.03
P5, Grandiosity	1.27	0.96	0.10	0.02
P6, Suspiciousness/Persecution	2.13	1.25	0.07	0.06
P7, Hostility	1.19	0.57	0.15	– 0.00
N1, Blunted Affect	2.85	1.38	0.08	0.05
N2, Emotional Withdrawal	2.71	1.34	0.17	0.10
N3, Poor Rapport	2.60	1.27	– 0.08	0.08
N4, Passive Social Withdrawal	3.04	1.47	– 0.00	– 0.07
N5, Difficulty in Abstract Thinking	2.79	1.38	– 0.12	– 0.05
N6, Lack of Spontaneity	2.58	1.44	– 0.03	– 0.09
N7, Stereotyped Thinking	2.44	1.32	0.07	– 0.16
ESI, Attention/Speech Impairment	6.73	5.74	– 0.33*	0.16
ESI, Ideas of Reference	4.06	4.21	– 0.09	0.00
ESI, Auditory Uncertainty	4.71	4.98	– 0.53***	– 0.05
ESI, Deviant Perception	4.15	4.64	– 0.29*	– 0.20

***: $p < 0.001$; **: $p < 0.01$; *: $p < 0.05$

Tab. 3 Relationship (Rho) between neuroleptic medication and SoA performance

	SoA Performance	
	Left VF	Right VF
Total NL dose (N = 48)	– 0.27 (*)	– 0.32*
Typical NL only (N = 17)	0.06	– 0.30
Atypical NL only (N = 26)	– 0.41*	– 0.19

*: $p < 0.05$; (*): $p < 0.1$

Discussion

Schizophrenics and controls both showed a better SoA performance for the right VF; this is in line with the usual finding that the left brain hemisphere is superior in processing verbal stimuli, e. g., listening or reading (Worral and Coles 1976; see Kandel et al. 1991).

The present study failed to replicate SoA performance group differences between schizophrenics and controls. A possible explanation refers to the matching technique; since schizophrenic illness can compromise a subjects ability to reach his/her premorbid educational expectation, the matching of schizophrenics and controls for *observed* educational level may result in the selection of controls with a lower educational *potential* (and presumably a lower level of cognitive functions) compared to schizophrenic patients. Hence, a possible SoA impairment of the schizophrenic group may have been obscured by a group imbalance between educational potential. An alternative strategy would have been to match subjects for parental levels of education, occupation and socio-economic status, all of which provide estimates of premorbid educational expectation. However, other studies showing significant SoA impairments of schizophrenics also used the educational level of patients and controls for group matching (e. g., Elkins et al. 1992).

The lack of group differences may be due to differences between the used SoA task procedures (e. g., subtle characteristics of the stimuli; see Sergent and Hellige 1986). However, the difficulty level of the present SoA task (around 75 % of correct performance) corresponds with that of former studies (e. g., Strauss et al. 1993; Elkins et al. 1992; Granholm et al. 1996). Furthermore, using the computerized UCLA version of the SoA (Asarnow and Nuechterlein 1994), Suslow and Arolt (1997) also reported the absence of group differences between schizophrenics, depressives, and healthy controls.

There is evidence that sensitivity and specificity of the Estes and Taylor task to schizophrenic disorder is influenced mainly by two features: the complexity of the task and the visual angle of the display. As Asarnow and Granholm (1991, p 208) pointed out, especially task versions which are characterized by complex conditions (8 or more letter stimuli) and a wide visual angle (9.5° × 10° or wider) seem to distinguish schizophrenics and normal controls, while other parameters (e. g., luminance and duration of the stimulus presentation) have little effect. Accordingly – and in correspondance with the recommendations of Asarnow et al. (1991) – our SoA procedure uses an 8-letter condition and a wide visual angle.[2]

The observation that the only significant correlations between SoA and schizophrenic psychopathology concern the left VF supports theories that suppose a deficit of the right cerebral hemisphere for schizophrenia (Venables 1984; Cromwell 1987; Cutting 1994). Especially the highly significant relationship of "Hallucinatory Behavior" (PANSS) and "Auditory Uncertainty" (ESI) with

2 In a recent study by Granholm et al. (1996) schizophrenics were best discriminated from nonpsychiatric subjects with a narrow angle SoA condition.

left VF SoA performance corresponds with hypotheses that auditory hallucinations might arise from right-hemisphere dysfunction (Randall 1983; Cutting 1990; for a review see David 1994). Former studies showed relations between SoA performance and negative symptoms rather than positive symptoms. However, relations between SoA deficits and psychopathology may depend on the duration of illness. Negative symptoms are known to increase with the course of the schizophrenic disorder. Since first psychiatric admission of the patients in the present sample were in the mean not more than four years ago, they may not have developed negative symptoms as much as chronic schizophrenics included in other studies. In any case, a finding of four significant correlations out of 36 possible should be interpreted with reservations, all the more because no SoA performance group differences were found.

Since this study was not designed to examine psychopharmacological effects, the results referring to this also should be considered cautiously. Patients were not randomized to medication groups; e. g., atypical NL were mainly given to patients, which turned out to be refractory to typical NL therapy. Hence, the NL subgroups in the present study may differ regarding the underlying pathophysiology. This is also suggested by the fact that patients receiving atypical NL had more negative symptoms than patients receiving typical NL.

The negative relationship between SoA performance and NL dosage (Table 3) corresponds with earlier findings of Spohn et al. (1985). The moderate correlation between atypical NL dosage and left VF SoA performance indicates that atypical NL may be related to right-hemispheric functioning, suggesting that the mechanisms of action of atypical NL are located mainly in the right hemisphere. Of course, this conclusion is highly speculative. Up to now, neither the nature of the effects of clozapine and newer atypical NL on cognitive processes nor their mechanisms of action have been fully explained (Hawkins et al. 1999). Beneficial effects of atypical NL on neuropsychological functions have been reported (Buchanan et al. 1994) as well as negative effects (Ragland et al. 1996).

All considered sociodemographic variables had a significant effect on SoA: young subjects performed better than old subjects (both VFs), males performed better than females (only right VF), and subjects with high education performed better than subjects with low education (only right VF).

The finding of gender differences in cerebral organization for language is well-established; e. g., language seems to be less lateralized in women (McGlone 1980). This may cause a left-hemispheric advantage of males in processing verbal stimuli. Nevertheless, the precise interpretation of the gender effect remains unclear; but this result underlines the need to take account of gender effects in future SoA studies.

The SoA task is based on the detection of tachistoscopically presented letters and, therefore, obviously demands fast reading. A subjects speed of reading will be influenced by his or her familiarity with written language (e. g., books, newspapers). Probably the educational level reflects this familiarity and, therefore, is related to SoA performance as described. On the other hand, differential attentional capacities could account for differential SoA performance as well as for differential success in education. In either case, since schizophrenic samples mostly show a reduced school education, the strong dependence of right VF performance on school education confirms the necessity for a careful education-matching of control groups.

Altogether, the findings of the present study indicate the need for further basic research on the span of apprehension paradigm. Relevant questions concern, among other things, the specificity of SoA deficits to schizophrenia, the associations between SoA performance and schizophrenic psychopathology, effects of antipsychotic medication (especially atypical NL), and the different roles of the left and right brain hemisphere for the SoA performance.

Acknowledgments This research was supported by the German Research Society (grant Ma 1765/1). The authors wish to thank Dr. Christian Haasen for the grammatical correction of the manuscript.

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