Mixed handedness is associated with the Disorganization dimension of schizotypy in a young male population

Nicholas C. Stefanis, Silia Vitoratou, Nikos Smyrnis, Theodoros Constantinidis, Ioannis Evdokimidis, Ioannis Hatzimanolis, Ioannis Ntzoufras, Costas N. Stefanis

Abstract

Within the ASPIS (Athens Study of Psychosis Proneness and Incidence of Schizophrenia) we sought out to examine in accordance with previous reports if a deviation from dextrality is associated with an augmented endorsement of self rated schizotypal personality traits in a large population of 1129 young male army recruits. Schizotypal traits were assessed using the Schizotypal Personality Questionnaire and hand preference membership was determined by applying stringent criteria derived from the Annett Handedness Questionnaire and the Porac–Coren questionnaire of lateral preferences. By adopting three different definitions of hand preference membership, we confirmed an association between mixed handedness and increased schizotypal personality traits, and in particular with Disorganization schizotypy that encompasses aspects of self perceived difficulties in verbal communication. Non-verbal cognitive ability, as indexed by measurement of non-verbal IQ, sustained attention and working memory was not associated with hand preference. We argue that a deviation from normal cerebral lateralization, as indexed by mixed handedness, is associated with mild sub clinical language dysfunction, rather than non-verbal cognitive ability, and this might be relevant to the expression of psychosis phenotype.

Keywords: Cerebral lateralization; Mixed handedness; Schizophrenia; Schizotypy; SPQ

1. Introduction

As a proxy measure of decreased cerebral lateralization, mixed handedness or ambitaxiality has been associated in many studies with schizophrenia and elevated schizotypy scores in non-clinical samples, thus reinforcing the notion that subtle disturbances in the establishment of normal cerebral asymmetry, might to some extent be related to the etiology of the disorder (Flor-Henry, 1969; Crow et al., 1989) and/or symptom expression within the psychosis extended phenotype (Barnett and Corballis, 2002; Chapman and Chapman, 1987; Claridge et al., 1998; Dollfus et al., 2002; Gregory et al., 2003; Kim et al., 1992; Manoach et al., 1988;
Manoach, 1994; Poreh, 1994; Shaw et al., 2001; Sperling et al., 1999). Several studies however, have failed to confirm the schizotypy–handedness relationship (Dinn et al., 2002; Dragovic et al., 2005; Jaspers-Manoach et al., 1999). Numerous confounding factors may account for these discrepancies across studies ranging from different definitions and methods of assessment of mixed handedness, to differences in population characteristics. The primary aim of this study was to examine if mixed handedness assessed by three different definitions of hand preference membership, is associated with the dimensional endorsement of self rated schizotypal personality traits in a large sample of young male conscripts who are representative for the Greek population of this age stratum. Since it has been debated if cerebral lateralization processes may correlate with cognitive ability (Annett and Manning, 1989, 1990; Leask and Crow, 2005) we wished to examine further if hand preference discriminates conscripts on non-verbal cognitive performance.

2. Methods

2.1. Participants

Participants were volunteers drawn randomly from eight consecutive draft board presentations of young conscripts aged 18–24 at the recruitment center of the Air Force military base, as part of the ongoing ASPIS study (Athens Study of Psychosis Proneness and Incidence of Schizophrenia; Stefanis et al., 2004a). Military service is compulsory in Greece and all healthy males are recruited and assigned to the different army corps by random assignment. All conscripts had been evaluated as not suffering from a major medical condition. The study was approved by The Bioethics and Medical Deontology Committee of the University Mental Health Research Institute. The initial sample consisted of 1353 conscripts who had reliable completed the Schizotypal Personality Questionnaire (SPQ; Raine, 1991), of which 1129 (83.4%) demonstrated hand preference for the 6 primary actions derived from the Annett (1970) Hand Preference Questionnaire (HPQ) and 947 conscripts (70%) demonstrated in addition, hand preference for actions derived from the Porac and Coren (1981) questionnaire of lateral preferences (P/C).

2.2. Handedness assessment

The 6 primary actions in the HPQ consist of hand preference for writing, throwing ball, hammering nail, brushing teeth, striking match, and holding a racquet. The six secondary actions defined in the HPQ were not assessed. Responses were coded as “right”, “left”, or “either” to each action. Based on his response pattern to the 6 primary actions, each conscript was assigned to one of three classes “right”, “left”, or “mixed” according to the following two definitions of hand preference.

A) In adherence to Annett’s (1970, 1985) recommendation, responses of “either” were coded as the writing hand and mixed handed individuals were defined as anyone demonstrating right or either preference for writing but left hand preference for any other primary action (original class 5) and any individual demonstrating left or either preference for writing but right hand preference for any other primary action (original class 6). We combined classes 5 and 6 into a mixed handedness group. We therefore adopted a narrow definition of mixed handedness since it has been suggested that this would best capture the “point of hemispheric indecision” that Crow (1997) claims is a core feature of schizophrenia. Individuals belonging to the original Annett classes 1–4 were grouped and defined as right handed and individuals belonging to the original Annett classes 7 and 8 were grouped and defined as left handed.

B) We further opted for an alternative a-theoretical but data oriented exploratory approach for hand preference membership utilizing Cluster Analysis methodology (Hierarchical clustering, Average Linkage between groups comparison; Anderberg, 1973). Peters and Murphy (1992) have suggested that it is possible to produce distinct groups of handedness by using cluster analytical methods. The two initial left and right handed groups were defined as in the previous categorization; the remaining 323 subjects were assigned to three groups according to cluster analysis methodology. The central group was defined as the mixed handed, while the other two groups were defined as right and left handed groups and therefore were added to the corresponding initial groups.

C) Handedness was in addition, assessed by direct demonstration to the four actions (throwing ball, drawing, erasing and removing top card while dealing) derived from the P/C questionnaire. Each action demonstrated with the left hand was coded as −1, with the right hand as 1 while actions using either hand were coded by zero. The scores for each individual in all tasks were summed and divided by 4 (the number of tasks). The conscripts whose final scores were −1 and −0.5 were coded as left handers, the ones whose scores were 0.5 and 1 were coded as right and the ones with middle scores (−0.3 and 0.3) formed the mixed handed group.
We also used a dichotomous definition of handedness by dividing individuals in two mixed and non-mixed (right and left) groups, based on the previous three hand membership definitions.

2.3. Schizotypy assessment

The SPQ is a 74-item questionnaire that assesses all nine aspects of the Schizotypal Personality Disorder (SPD) according the Diagnostic and Statistical Manual of Mental Disorders Revised (DSM-III-R; American Psychiatric Association, 1987). The analysis of the factorial structure of the SPQ as defined by the responses of the Greek sample has been assessed through confirmatory factor analysis and indicated that the best fit to the data was provided by a four factor model namely Positive, Negative, Disorganization and Paranoid factor (Stefanis et al., 2004a).

2.4. Non-verbal cognitive ability assessment

Conscripts underwent an extensive interview of computerized neurocognitive abilities including assessment of vigilance with the Continuous Performance Task-Identical Pair version (CPT-IP; Cornblatt et al., 1988, 1989), verbal and spatial working memory with a version of N-Back (Gevins et al., 1996) and non-verbal IQ was estimated with Raven Progressive Matrices (RPM; Raven, 1988). For each of the three computerized cognitive task, the central index of performance ($d'$) was used in subsequent analyses as described previously (Stefanis et al., 2004b). Nine hundred and twenty-five conscripts (81.2%) had valid measures on all four cognitive tasks.

2.5. Statistical analysis

The normality assumption was rejected in all cases (Lilliefors, 1967; Kolmogorov–Smirnov Test of Normality: $p > 0.05$). Hence, the corresponding non-parametric Kruskal–Wallis test (KW $\chi^2$) was used, followed by Dunn (1964) post hoc tests for pairwise comparisons. For the comparisons of the mixed with the non-mixed individuals the Wilcoxon/Mann–Whitney (MW U) test was used. The agreement between the 3 alternative memberships and the test–retest reliability of the HPQ were assessed by Cohen’s (1960) Kappa coefficient. All data analyses were conducted on the SPSS 10.0 statistical package.

3. Results

3.1. Comparison of schizotypy scores across hand preference membership

Using the Annett hand preference membership, based on the 6 primary actions, 974 conscripts (86.3%) were assigned in the right-handed group, 92 conscripts (8.1%) were assigned in mixed group and 63 conscripts (5.6%) were assigned to the left handed group.

When the Cluster analysis approach to hand preference membership was used, 1003 cases (88.8%) were assigned to the right handed group, 50 cases (4.4%) were assigned to the mixed handed group and 76 cases (6.7%) to the left handed group.

Using the P/C criteria for hand preference membership, 839 (74.3%) individuals were classified as right handers, 46 (4.1%) as mixed handers and 62 (5.5%) as left handers.

### Table 1

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<td>Annett (N=1129)</td>
<td>Right</td>
<td>0.199 (0.11)</td>
<td>0.180 (0.12)</td>
<td>0.414 (0.20)*</td>
<td>0.441 (0.19)</td>
<td>36.752 (16.73)</td>
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<td>0.474 (0.18)</td>
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<td>Left</td>
<td>0.218 (0.11)</td>
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<td>0.484 (0.17)</td>
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<td>0.202 (0.11)</td>
<td>0.183 (0.12)</td>
<td>0.420 (0.20)</td>
<td>0.447 (0.18)</td>
<td>37.286 (16.69)</td>
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<td>0.443 (0.18)</td>
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<td>Mixed</td>
<td>0.223 (0.12)</td>
<td>0.201 (0.12)</td>
<td>0.473 (0.19)</td>
<td>0.467 (0.18)</td>
<td>40.201 (16.42)</td>
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<td>Left</td>
<td>0.211 (0.11)</td>
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<td>0.456 (0.19)</td>
<td>0.487 (0.17)</td>
<td>40.696 (16.03)</td>
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<td>0.183 (0.12)</td>
<td>0.420 (0.20)</td>
<td>0.447 (0.18)</td>
<td>37.286 (16.69)</td>
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<td>Porac–Coren (N=947)</td>
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<td>0.444 (0.18)</td>
<td>37.012 (16.55)</td>
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<td>Mixed</td>
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<td>0.198 (0.12)</td>
<td>0.483 (0.18)*</td>
<td>0.484 (0.17)</td>
<td>40.691 (15.36)</td>
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<td>Left</td>
<td>0.209 (0.11)</td>
<td>0.187 (0.11)</td>
<td>0.438 (0.19)</td>
<td>0.477 (0.17)</td>
<td>38.981 (16.16)</td>
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<td>Total</td>
<td>0.201 (0.11)</td>
<td>0.184 (0.12)</td>
<td>0.421 (0.20)</td>
<td>0.448 (0.18)</td>
<td>37.319 (16.48)</td>
</tr>
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</table>

a, b, c, d, e The scores of the three groups within columns were significantly different according Kruskal–Wallis test ($p < 0.05$).

* The scores of the two groups were significantly different according Dunn post hoc test ($p < 0.017$).
left handers. The definition of mixed handedness according to Annett hand preference membership was the least stringent of the three, since only 46% and 41% of these individuals, were also characterized as mixed handed by cluster analysis and P/C criteria respectively.

No differences in age, and years of education emerged between the three handedness groups in either of three hand preference memberships. The degree of agreement on class status between the three definitions of hand preference assessed with Kappa statistics and found by pair wise comparisons greater than 0.71 indicating good and high agreement between the three definitions of hand preference membership (Landis and Koch, 1977).

Significant differences between the three handedness groups according to the Annett hand preference membership emerged for the Disorganization SPQ factor and for the total SPQ score (Tables 1 and 2). In the cases of the other three factors the differences were evidential of a trend ($p<0.10$), with the Positive and Negative factors being marginally significant (Table 2). The pairwise comparisons were also assessed using the Dunn test (1964). In all comparisons, the significance level was set up to $\alpha=0.10$ concluding to significance level $\alpha'=0.017$ for each paired comparison. The Dunn test yielded significant difference in the case of the scores of the Disorganization factor between right and mixed handers ($p=0.012$) with mixed handed individuals scoring higher (Table 1).

The comparisons of the SPQ schizotypy scores between the three handedness groups using the cluster analysis methodology (Tables 1 and 2), led us to similar conclusions in the cases of the Disorganization factor and total SPQ scores. However, Dunn test did not yield any significant pairwise differences. The differences in the scores between the three handedness groups were marginally significant for the other SPQ factors (Table 2).

Replicating previous analyses by applying the P/C definition of hand preference membership, significant differences were observed for the Disorganization factor. None of the other SPQ factors (Positive, Negative, or Paranoid) or the total SPQ score differed significantly amongst the three handedness groups defined by P/C criteria.

At the 9 SPQ subscale level, ‘odd speech’ was the subscale that was most persistently associated with significant differences ($p<0.05$) between the three handedness groups (data not shown).

The mixed handedness group had significantly higher scores than the non-mixed, on the Disorganization SPQ factor in all dichotomous defined handedness groups (Tables 3 and 4). Significant differences in the scores of the SPQ Positive factor among mixed and non-

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### Table 2

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<td>5.85</td>
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<td>2.91</td>
<td>5.45</td>
<td>7.55</td>
<td>4.80</td>
<td>6.06</td>
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<tr>
<td></td>
<td>df</td>
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<td>2</td>
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<tr>
<td></td>
<td>p-value</td>
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<td>0.066</td>
<td>0.023</td>
<td>0.091</td>
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<tr>
<td>Porac-Coren ($N=947$)</td>
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<td>3.80</td>
<td>3.23</td>
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<td></td>
<td>df</td>
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<tr>
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<td>p-value</td>
<td>0.216</td>
<td>0.558</td>
<td>0.042</td>
<td>0.150</td>
<td>0.198</td>
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</table>

* Kruskal–Wallis Chi-Square.
mixed handed groups was noted only using the Annett hand preference membership.

No significant differences between mixed and non-mixed handedness groups were observed for the total SPQ score, the Negative and Paranoid SPQ factors.

3.2. Test–retest of Annett membership

Two years after the initial assessment, a sub-sample of 260 conscripts was summoned to participate in a retest analysis including hand preference on the 6 primary actions. The Kappa coefficient on class membership was 0.784 (p<0.001), indicating high agreement between the two assessments of individual’s hand preferences.

3.3. Non-verbal cognitive ability and hand preference membership

No differences in non-verbal cognitive ability were found across the three handedness groups (right, mixed, left) according to the Annett hand preference membership (CPT-IP: KW $\chi^2$=0.29, df=2, p=0.869; verbal N-Back: KW $\chi^2$=0.66, df=2, p=0.717; spatial N-Back: KW $\chi^2$=0.248, df=2, p=0.883; Raven PM scores: KW $\chi^2$=0.64, df=2, p=0.726). Likewise, no differences emerged when hand preference membership was defined either by cluster analysis or by P/C criteria. Additionally, mixed versus non-mixed handedness groups did not differ in terms of non-verbal cognitive ability.

4. Discussion

Our results indicate that self rated schizotypal personality traits are sensitive to hand preference which is considered an indirect marker for the degree of cerebral lateralization. Significant differences of the total SPQ scores were found between the three groups of hand preference defined by theoretical and data oriented approaches. Disorganization schizotypy was the most sensitive SPQ dimension to hand preference. This dimension was consistently associated with mixed handedness regardless of hand preference classification. The association was even more significant as more stringent criteria for mixed handedness were applied (Table 4). The Disorganization SPQ factor encompasses the subscales of ‘odd speech’ and ‘odd behavior’, and contains items related to self perceived difficulties in oral communication, and oddities in social behavior. The significant association between ambitextrality and oddities in verbal communication within apparently healthy individuals supports the validity of previous reports according to which lateralization is a determinant of verbal abilities in the general population (Crow, 1998; Leask and Crow, 2005). In these studies, equal hand skilled children had relatively more verbal deficits, analogous perhaps to the deviations in verbal communication reported by ambidextrous conscripts in this study.

The association between mixed handedness and Disorganization schizotypy reported here is reminiscent of the corresponding association between mixed handedness and formal thought disorder in schizophrenia (Dollifus et al., 2002; Manoach, 1994). It may be viewed therefore, under a dimensional perspective where deviant cerebral lateralization, indexed by a preference for mixed handedness, interferes with language related processes. This relationship may act in such a way as to bias ambidextrous individuals towards language related dysfunction across a gradient of severity, ranging from relative mild deficits in verbal abilities and sub clinical oddities in verbal communication amongst apparently healthy individuals, as suggested in this study, to the manifestation of formal thought disorder in schizophrenia. According to this hypothesis, mixed handedness may constitute a risk factor for language related disorder across the spectrum (from schizotypy to schizophrenia) and is not necessarily related specifically to schizophrenia per se. Indeed it

Table 4
Mann–Whitney test of differences in the SPQ factor and total scores between non-mixed and mixed groups derived from the each hand preference classification

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<td>Annett (N=1129)</td>
<td>MW-U*</td>
<td>47,664.5</td>
<td>49,775.5</td>
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<td>24,440.5</td>
<td>21,910.5</td>
<td>24,568.5</td>
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<tr>
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<td>0.261</td>
<td>0.025</td>
<td>0.286</td>
<td>0.105</td>
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<tr>
<td>Porac–Coren (N=947)</td>
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<td>17,860.0</td>
<td>18,981.0</td>
<td>16,369.0</td>
<td>17,981.0</td>
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<td>p-value</td>
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<td>0.114</td>
<td>0.336</td>
<td>0.016</td>
<td>0.130</td>
<td>0.103</td>
</tr>
</tbody>
</table>

* Mann–Whitney U.
has been observed that lateralization problems incur risk for language delays and deficits including stuttering (Orton, 1937); as well as reading, spelling and drawing difficulties (Zangwill, 1960). Furthermore, mixed handedness has been associated with an increased risk for other language related disorders such as dyslexia (Richardson, 1994).

A bolder approach that views schizophrenia as a developmentally induced failure of lateralization of the components of language would adopt a slightly different interpretation of our finding. Mixed handedness and deficits in verbal abilities are viewed as combined markers of an underlying causal process, that is, failure of the hemispheric dominance for language, since they are over-represented in the disorder and in children destined to become ill (Crow, 1998; Leask and Crow, 2005). This hypothesis would imply that mixed handed individuals, high on Disorganization schizotypy would be at an increased risk to develop psychosis. Due to the 2-year prospective design of ASPIS, this hypothesis cannot be tested.

Ambidextrality was found to be associated to Disorganization rather than the Positive aspects of schizotypy, in contrast to several previous studies (Kim et al., 1992; Poreh et al., 1997; Shaw et al., 2001). Following the Annett hand preference classification, mixed handed individuals scored higher (than non-mixed) on Disorganization as well as positive aspects of schizotypy. This was the only significant association with positive schizotypy and hand preference in our analysis. Furthermore, and as opposed to Disorganization schizotypy, observed trends of association between positive and negative SPQ factors with mixed handedness disappeared, when more stringent definitions of mixed handedness were employed (by cluster analysis or P/C criteria) (Tables 2 and 4). It is therefore plausible that previous reported inconsistencies are to an extent dependent on broader definitions of mixed handedness. Moreover, a close inspection of previous work published on the association between mixed handedness and SPQ by Kim et al. (1992), Poreh et al. (1997) indicate that the strongest associations noted were with subscales ‘odd speech’, and ‘odd behavior and appearance’ respectively, both components of the Disorganization, rather than the positive schizotypy factor.

Although samples of students used in previous studies may reflect selected individuals due to higher academic achievement, cognitive ability and social background, caution should be exercised since the one study to date to assess schizotypy (measured with the SPQ) in a representative sample of the general community failed to show an association with mixed handedness (Dragovic et al., 2005). The focus on a male population may have contributed to the strengthening of the association between schizotypy and atypical handedness as described in previous studies (Gregory et al., 2003; Shaw et al., 2001).

Finally, mixed handedness was not associated with decreased performance on non-verbal cognitive tasks, supporting thus the notion that reduced cerebral lateralization, as indexed by mixed handedness, is more sensitive to subtle verbal manifestation of language processes rather than non-verbal cognitive ability.

5. Limitations

Handedness was assessed with demonstration on hand preference for the six primary actions and not for the six secondary actions defined by the 12 item AHQ scale, making comparability difficult with other studies on hand preference. We argue that in the full 12 item AHQ scale, the core mixed handedness groups (classes 5 and 6) that best capture the “point of hemispheric indecision” (Crow, 1997) are defined by the 6 primary actions alone, with no need to incorporate the secondary ones. Culturally enforced writing with the right hand in otherwise left handed individuals was not controlled for. Nevertheless, the lengthier the tasks performed, the higher the probability of establishing a task performed with the opposite hand from writing, a fact that may account for a high distribution of mixed handedness (30% of the population) when the 12 item questionnaire is used (Annett, 1972).

The predictive validity of schizotypy self rated scales has been questioned (Kendler et al., 1996). Moreover, it has been proposed that the Disorganization schizotypy factor encompassing oddities in speech and behavior cannot be self rated reliably and is frequently under-reported (Bergman et al., 1996; Kendler et al., 1996; Vollmea and Ormel, 1999). However, such a general under-reporting would have led to a bias towards the null rather than induce mixed non-mixed handedness differences. Thus, the assumption of under-reporting would confirm our results, unless one assumes that mixed handed conscripts were more self aware and accurate in reporting their behavioral and verbal communication difficulties compared to the non-mixed handedness group. Although it is unlikely that a presumable heightened self awareness would bias mixed handers to report more verbal related difficulties than say paranoid beliefs or interpersonal difficulties, the army recruitment environment, which demands quick responses to right–left commands, may confuse mixed handers more than non-mixed handers.
Acknowledgments

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References


