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Research Letter

Age does not explain high rates of minor physical anomalies in schizophrenia patients

In a study of healthy individuals Lloyd *et al*. (2003) reported higher rates of minor physical anomalies (MPA) among older (>60 years) than younger subjects. Based on these results they questioned the strong association between schizophrenia and MPA and argued that age might confound this relationship. Since Lloyd *et al*.'s conclusions challenge the relevance of MPA for schizophrenia, we retested the question of whether or not age is significantly related to MPA rates in subjects with or without schizophrenia in data from four independent samples in three countries. The total samples include 298 psychosis patients and 103 controls, with good representation throughout the adult age span of both sexes. The studies of Ismail *et al*. (1998), Kelly *et al*. (2005), and Lane *et al*. (1997) have previously shown strong associations between MPA and schizophrenia, while the Nesvåg *et al*. study (unpublished observations) constitutes preliminary results from ongoing research. If Lloyd *et al*.'s conclusions are correct and generalizable, one would predict increasing MPA rates with increasing age among both patients and controls and no difference in frequencies in MPA rates in schizophrenia *versus* control subjects of the same age.

Three of the four studies comprised 271 subjects who met DSM-III-R criteria for schizophrenia. The Nesvåg *et al*. study also included 27 patients with DSM-IV other psychoses. Exclusion criteria comprised no major neurological or somatic disorder or history of head trauma. All controls were free of mental illness. More information can be obtained from the corresponding references (Lane *et al*. 1997; Ismail *et al*. 1998; Kelly *et al*. 2005) and the first author of the Nesvåg *et al*. study.

The Ismail *et al*. study included 60 patients from Malmö, Sweden and measured MPA with items from the Waldrop *et al*. study (1968), as well as additional sources. The Kelly *et al*. study included 55 subjects (28 schizophrenia patients and 27 controls from Stockholm, Sweden), all subjects being examined using the Lane Scale (Lane *et al*. 1997). The Lane *et al*. study comprised 165 patients and 76 control subjects recruited from Dublin, Ireland, MPA measured with the Lane scale. Subjects in the Nesvåg *et al*. study were part of an ongoing study in Oslo, Norway. Thus far, 45 patients (18 with schizophrenia, and the remaining with other psychoses) have been selected, and MPA were assessed using a 10-item scale.

The notable variation in the composition of the psychosis samples and the MPA scales across the studies prohibited combining the data into one common dataset. For simplification of comparison, rates of total MPA rather than specific MPA were studied. The relationship between total MPA score and age was examined using Spearman's r_s for each sample in total, for patients and controls separately, and for men and women separately. There was no evidence that the association between MPA and age was influenced by gender, so no further stratification by gender was employed. The mean and standard deviation for total MPA were calculated *per each age quartile*. The Kruskal–Wallis test was used to analyse differences for total MPA by age quartiles, and linear trends were analysed using the Jonckheere–Tepstra test. Comparison of MPA means was done by Student's *t* test.

Results and comment

None of the rank correlation between MPA score and age in each sample (or gender, patient/control status subgroups) was close to statistical significance. Table 1 presents the mean MPA score by age quartiles for patients/controls. There was no significant change in MPA scores by increasing age and no significant trend over age quartiles. In the Lane *et al*. study, mean MPA were significantly higher in patients aged >60 years (53.7 ± 10.7) than in patients aged ⩽60 years (49.5 ± 8.6) ($p = 0.040$), while no such difference was seen in corresponding control groups (33.6 ± 8.9 *v.* 33.7 ± 8.2) ($p = 0.975$). The ratio for mean MPA in patients:controls (Table 1) remained stabile (1.49, 1.47,

Table 1. *Mean MPA score and standard deviation per age quartile for the participants in the four independent samples included in this study*

	1st age quartile	2nd age quartile	3rd age quartile	4th age quartile
Study[a]	MPA mean [S.D.] (*n*)	MPA mean [S.D.] (*n*)	MPA mean [S.D.] (*n*)	MPA mean [S.D.] (*n*)
Only patients				
Ismail *et al*. MPA score min 2, max 15	6.6 [3.5] (18)	5.9 [2.2] (14)	6.2 [1.8] (14)	6.8 [2.6] (14)
Kelly *et al*. MPA score min 1, max 26	14.4 [7.8] (9)	17.7 [5.4] (7)	14.8 [2.2] (5)	12.4 [8.5] (7)
Lane *et al*. MPA score min 31, max 90	50.7 [9.8] (36)	49.4 [8.2] (46)	48.6 [8.2] (50)	53.7 [10.7] (33)
Nesvåg *et al*. MPA score min 0, max 9	2.4 [3.2] (12)	2.9 [2.4] (13)	2.4 [2.4] (10)	2.6 [2.4] (10)
Only controls				
Kelly *et al*. MPA score min 0, max 13	5.2 [5.3] (5)	4.0 [2.8] (9)	4.6 [3.9] (8)	4.4 [4.0] (5)
Lane *et al*. MPA score min 16, max 66	34.1 [6.1] (26)	33.5 [11.6] (13)	32.8 [8.5] (10)	33.6 [8.9] (27)

MPA mean, Mean for the minor physical anomalies score for each sample; S.D., standard deviation.
Ismail *et al*. study: 1st age quartile 19–33 yr, 2nd age quartile 34–39 yr, 3rd age quartile 40–45 yr, 4th age quartile 46–55 yr.
Kelly *et al*. study: 1st age quartile 23–37 yr, 2nd age quartile 38–44 yr, 3rd age quartile 45–47 yr, 4th age quartile 48–50 yr.
Lane *et al*. study: 1st age quartile 18–30 yr, 2nd age quartile 31–44 yr, 3rd age quartile 45–60 yr, 4th age quartile 61–89 yr.
Nesvåg *et al*. study: 1st age quartile 18–23 yr, 2nd age quartile 24–27 yr, 3rd age quartile 28–30 yr, 4th age quartile 31–47 yr.
[a] Min(imum) and max(imum) refer to lowest and highest scores that occurred in that sample.

1.48) across the first three age quartiles but increased (to 1.60) in the oldest quartile.

In the literature, we found 11 frequently cited studies providing evidence for the existence of an increase in MPA among schizophrenia patients. Two of these did not, however, present the participants' age. Subject age was <55 years in five studies and <60 years in one further study. Of the remaining studies that included subjects aged >60 years, two actually had higher mean age for the controls than patients, while the third study showed no age differences.

No significant relationship was observed between MPA rate and age across all ages in any study. Patients (but not controls) aged >60 years had significantly but modestly increased MPA scores, paralleling Lloyd *et al*.'s finding in normal controls of similar age. With greater power this might point towards a possible increase of MPA in *all* older ages, but it would not explain the consistent differences in rates of MPA in schizophrenia patients, compared to equally aged controls. If it were of interest to investigate the frequencies of MPA in schizophrenia subjects aged >60 years, it would require a study design which includes older subjects with and without schizophrenia.

A literature search was done in order to determine whether the apparent increase of MPA in subjects aged >60 years represents a true confounding in the studies constituting evidence for the association between MPA and schizophrenia. Only three of the nine studies that were identified included subjects aged >60 years, and the mean age of schizophrenia patients was lower than, or the same as, that for controls.

Thus, nothing suggests that high subject age provided a confounding towards increased MPA rates in schizophrenia patients. The current findings give no reason to reconsider earlier consistent and robust

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findings of increased rates of MPA in schizophrenia *versus* controls in a number of studies over the years.

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Declaration of Interest

None.

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