Title:

Greater number of older siblings is associated with decreased theory of mind ability in psychosis.

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Dear Editors,

Deficits in social information processing are core features of several disorders of mental health, including schizophrenia (SZ), and often better predict functional outcomes in employment and relationships than neurocognition alone (Fett et al., 2011, Lam et al., 2014). Among these, Theory of Mind (ToM) - the ability of an individual to attribute a mental state to oneself or to others - has received significant research attention, partly on account of its association with a number of SZ genetic risk variants (Martin et al., 2014). Among suggested early social environmental factors, the effect of growing up with greater or fewer siblings has received little attention, despite being relatively easy to measure. In the non-SZ literature, better theory of mind ability has been associated with greater number of older but not younger siblings, or twins (Cassidy et al., 2005, Ruffman et al., 1998); this has been attributed to the modelling of theory of mind by older siblings during interaction, and parental demonstration of theory of mind during sibling conflict resolution (Tucker et al., 1999). In this context, the present study sought to determine whether number of older siblings was associated with variation in theory of mind performance in patients with either schizophrenia and schizoaffective disorder (N=196) and a broader psychosis group (N=75); consisting primarily of those with affective psychotic disorders (bipolar disorder and major depressive disorder with psychotic features).

Diagnosis was confirmed using the *Structured Clinical Interview* for DSM-IV *(SCID)* (First et al., 1995) and symptom severity using the SAPS and SANS. Neuropsychological function was assessed based on measures of general cognitive function, episodic and memory working memory and attentional controls using subtests from the Wechsler scales, CANTAB, and the CPT-IP respectively and as described previously (Donohoe et al., 2009). Theory of Mind was measured using the Reading the Mind in the Eyes test (Eyes Test; Baron-Cohen et al., (2001)); the total correct score served as the dependent measure. Demographic characteristics of the participants, including number of older siblings, are shown in Table 1.

**Table 1.** *Participant demographic characteristics*

|  |  |  |  |
| --- | --- | --- | --- |
|  | All patients | SZ or SZA | Other Psychosis |
| n | 271 | 196 | 75 |
| Age | 45.82(12.30) | 45.51(12.26) | 46.63(12.46) |
| Female % | 36.5 | 31.6 | 50 |
| No. of Older Siblings | 2.31 (2.36) | 2.26(2.40) | 2.47(2.24) |
| Eyes Test score | 20.56(6.45) | 19.79(6.51) | 22.57(5.86) |

SZ, schizophrenia; SZA, schizo-affective disorder; Eyes Test, Reading the Mind in the Eyes test. Data are given as mean (standard deviation).

Theory of Mind, as measured by the Eyes Test, was observed to be significantly negatively correlated with age, such that older patients had lower Eyes Test scores (Pearson's r = - 0.22; p = 0.000). No difference between males and females in Eyes Test score was observed for the total sample, although in the 'Other Psychosis' group, a trend-level difference emerged, such that men perfomed slightly better than women (t(72) = 1.97; p = 0.053). Using a one-way ANCOVA, in which age and gender were entered as covariates, to compare Eyes Test scores between diagnostic categories ('Schizophrenia/Schizoaffective' versus 'Other Psychosis'), the 'SZ/SZA' group obtained significantly lower scores than the 'Other Psychosis' group on the Eyes Test (SZ/SZA: M = 19.79, S.D. = 6.51; Other Psychosis: M = 22.57, SD = 5.86; F = 10.484, *p* < p = 0.001), in keeping with previous studies (Donohoe et al., 2012, Guastella et al., 2013).

After establishing a normal distribution within the dataset, we next sought to determine the relationship between Eyes Test performance and the number of older siblings of the proband. Using Pearson's r, a significant negative correlation was observed between Number of Older Siblings and Eyes Test scores, for both the sample as a whole (r = - 0.205, *p*

< 0.001, N = 271), and the subsamples of SZ/SZA (r = - 0.182, *p* < 0.01) and Other Psychosis (r = - 0.324, *p* < 0.01). In a regression analysis based on the total sample, in which Eyes Test scores were used as the dependent variable, and age and gender were entered on the first step, followed by number of older siblings on the second step, both age and number of older siblings (but not gender) independently contributed to variance explained in Eyes Test

performance (F(1,187) = 4.6; p = 0.033). Similar findings were observed when the SZ/SZA and Other Psychosis group were considered separately (SZ/SZA: F = 3.6, *p* = 0.013; Other Psychosis: F = 5.4, *p* = 0.012). Across these analyses, the amount of variance explained by Number of Older Siblings was modest (ranging from 2-3%). Finally, when we re-ran the analysis using Total Number of Siblings rather than Number of Older Siblings, a similar amount of variation in Eyes Test performance was observed (F = 6.85; p = 0.009; r2 = 2.7).

In summary, our hypothesis, based on previous literature in healthy controls, that better ToM performance would be associated with larger numbers of older siblings, was not supported (Lewis et al., 1996, McAlister & Peterson, 2013, Perner et al., 1994, Ruffman et al., 1998, Tucker et al., 1999). Instead, and contrary to expectations, a negative correlation was observed such that increased number of older siblings was associated with poorer theory of mind performance as measured by the Eyes Test. This held true for both 'SZ/SZA' group and the 'Other Psychosis' groups. This finding is however consistent with a study of children with Autistic Spectrum Disorder (ASD) where having at least one older sibling was associated with poorer ToM performance (O'Brien et al., in 2011). The authors suggest that this was a result of benefits, experienced by the eldest ASD children, of more attuned and more immediate attention from parents on account of their disorder. They further suggested that older siblings impede the development of younger ASD children as a result of over- compensatory assistance. However, given that many who experience psychosis are largely asymptomatic until early adulthood, this is unlikely to explain our results. Instead, we suggest that for individuals who later develop psychosis, and may already experience subtle difficulties with social adjustment, reduced ToM may in part result from a struggle with more complex social environments. This interpretation is speculative given our earlier hypothesis and warrants further investigation; however, support for this hypothesis derives from the fact that we observed comparable results when we used Total Number of Siblings as a predictor instead of Number of Older Siblings. In any event, we conclude that given the need to integrate genetic and early social environmental factors in order to understand social adjustment in schizophrenia, birth order is a potentially important variable.

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**\*Conflict of Interest**

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The authors declare no conflict of interest.

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