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Gender, psychopathology, and development: from puberty to early adulthood

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Abstract

We tested the hypothesis that the expression of schizophrenic psychopathology is dependent on the stage of adolescent development. The study had a retrospective design, using high-quality case-note material of cases of schizophrenia at first admission. Patients with onset of illness between the age of 11 and 21 years were included. Sexual delusions were more apparent in females (OR = 3.6;95% CI 1.6–8.0), but otherwise no gender differences in the frequency of a range of positive symptoms were apparent. There was evidence that the age at which positive symptoms first appeared differed between males and females. The frequency of typical, 'first rank' schizophrenic symptoms such as auditory hallucinations, passivity phenomena and thought interference, increased linearly with age in male patients, but did not vary with age in their female counterparts. The likelihood of displaying delusional beliefs such as persecutory delusions, explanatory delusions, delusions of reference and grandiose delusions increased with age in both sexes, but the association was stronger in males. The observation that typical schizophrenic symptoms in male patients are relatively uncommon during early adolescence, but increase as they grow older, could be explained by the later manifestation of puberty and associated maturational processes in boys.

Key words: Gender; Psychopathology; Development; (Schizophrenia)

1. Introduction

A developmental influence on the psychopathology of psychotic disorders in childhood and adolescence has been described by several authors. Psychotic symptoms tend to be relatively crude and poorly elaborated at an early age, compared with those described in older subjects (Kolvin et al., 1971; Russel et al., 1989; reviews by Tsiantis et al., 1986; Werry, 1992). However, comparisons using detailed psychopathological measures over an extended age range have been lacking, and while the disparities in psychopathology between childhood and adolescent schizophrenia on the one hand, and adult schizophrenia on the other are considered quantitative rather than qualitative by some (Werry, 1992), these differences have not yet been subject of evaluative research.

The neurodevelopmental hypothesis of schizophrenia postulates that developmental events in the brain underlie the emergence of psychotic symptoms (Feinberg, 1982/83; Weinberger, 1987; Murray et al., 1988; Saugstad, 1989). Because early adolescence is a period of profound matura-

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tional changes, many have speculated that the process of puberty triggers the events that produce psychosis. Such theories are compatible with the massive increase in the incidence of psychotic conditions seen around and after puberty, and with highly significant changes in the sex ratio around puberty, indicating that age of onset figures are closely mirrored by the timing of maturational processes (Kraepelin, 1919; Bettes and Walker, 1987; Galdos et al., 1993a; Galdos et al., 1993b). We wished to investigate whether psychotic illnesses arising in this period of life are associated with a particular pattern of psychopathology. We hypothesized that positive symptoms would become more frequent with increasing age, and that males, analogous to gender differences in the timing of puberty, would 'lag behind' females in the development of positive schizophrenic symptoms between early adolescence and early adulthood.

2. Methods

2.1. Sample

Subjects were incident cases (first admissions) of psychosis, consecutively referred to hospital to (i) the adolescent unit, and (ii) the adult units. Both the adolescent and the adult samples have been described before in detail (Galdos et al., 1993a; Harvey et al., 1990; Jones et al., 1993). Briefly, the adolescent sample consisted of subjects (age range: 11–18 years) referred between 1976 and 1990 to the regional adolescent unit at the Maudsley and Bethlem Royal Hospital in South London, selected if their discharge summary indicated the presence of any psychotic symptom (i.e. delusion, hallucination or thought disorder) in clear consciousness. Adult cases of similarly defined functional psychosis, aged 16 to 60 years, who had taken part in a previous study (Harvey et al., 1990; Jones et al., 1993), were drawn from two cross-sectional samples of consecutive patients, admitted to the Maudsley and Bethlem Royal and King's College Hospital in South London.

All medical, nursing, social work, and occupational therapy notes of all adolescent patients, and of patients from the adult sample with onset of illness up to age 21 years, were scrutinized. Thus, the examined age of onset range was from age 11 to age 21 years. This age range was taken to include the period of the most important developmental processes of possible relevance to the onset of psychosis, such as typical pubertal changes (Marshall and Tanner, 1986), myelination in the corticolimbic circuitry during late adolescence (Benes, 1989), and developmental regression of excessive interneuronal contacts persisting into the second decade of life (Huttenlocher, 1979).

All correspondence and accessory information was also examined. The quality of note-taking in the Maudsley and Bethlem Royal Hospital and King's College Hospital is high, and histories and mental states are collected using a semi-structured interview (Institute of Psychiatry Training Committee, 1973).

Psychotic symptoms were defined as indicated by Wing et al. (1974), and were rated on a three point scale where 0 indicated that the symptom was absent, 1 that it was doubtfully present or was minimal in severity, and 2 that it was definitely present. In the analyses, only a rating of 2 was considered valid. Based on all available information, an estimate was made of the age of onset of the disorder. Onset was defined as the emergence of psychotic symptoms that were described with sufficient clarity to rate as 2.

2.2. Diagnosis

The Operational Criteria Checklist for Psychotic Illness (OCCPI; McGuffin et al., 1991) was completed for all patients. The OCCPI check-list is based on phenomenological descriptions in the Present State Examination (Wing et al., 1974), and covers a wide range of operational definitions of psychiatric conditions. The computer program OPCRIT (McGuffin et al., 1991) was used to analyze the OCCPI data. DSM-III-R diagnoses were grouped into affective psychoses (manic, bipolar and depressive psychoses), schizophrenia (including schizophreniform psychosis and schizo-affective psychosis), and atypical psychoses (any other psychosis). Reliability of DSM-III-R OPCRIT diagnosis between the two raters was

tested on a random sample of 20 subjects. Kappa was satisfactory at 0.69 for DSM-III-R diagnoses.

2.3. Psychopathology

In order to reduce the amount of information provided by the individual psychotic symptoms, symptoms were grouped together into syndromes, according to the PSE Syndrome Checklist (Wing et al., 1974), with some modifications. Only positive symptoms which occurred with a frequency of 10% or higher were included in the analyses.

Thus, the following syndromes were identified: (i) auditory hallucinations; (ii) passivity phenomena; (iii) thought interference (thought withdrawal, thought broadcasting, thought insertion); (iv) explanatory delusions and fantastic delusions (delusions involving hypnotism, physical forces, alien forces, fantastic themes); (v) sexual delusions (including delusions of pregnancy); (vi) delusions of reference (delusions of reference and misidentification); (vii) persecutory delusions; (viii) grandiose delusions (including religious delusions); (ix) depressive delusions (delusions of guilt, hypochondriasis, catastrophe, nihilistic delusions). The kappa for these nine syndromes, using the same random sample of twenty subjects, was high (mean: 0.86; range: 0.73–1.00).

2.4. Analyses

Analyses were conducted with the EGRET statistical software (version 0.26.6, Statistics and Epidemiology Research Corporation, North Carolina, USA). The nine psychopathological syndromes were the binary response variables, and associations with sex and age of onset (as five consecutive age of onset groups) were examined in logistic regression models. First, age of onset and gender were entered together, so that the effect of each could be examined while adjusting for the other. Odds ratios and 95% confidence intervals for the explanatory variables were calculated from the result of the logistic regression (Breslow and Day, 1980). Subsequently, the model was extended with gender by age of onset interactions, and tested for significance using the likelihood ratio statistic. Stratified analyses were performed if there was evidence of significant interaction, using classical epidemiological methods, such as those of Mantel and Haenszel (1959). Kappas were calculated with the SPSS for Windows software (Norušis/SPSS Inc., 1990).

3. Results

3.1. The sample

The sample consisted of 180 subjects (97 from the adolescent unit, 83 from the adult units); 106 (59%) were male, and 74 (41%) female. Two subjects in the adolescent sample were described as pre-pubertal. One hundred and fourty-seven subjects (82%) had a diagnosis of broadly defined schizophrenia (males: 60%), 20 (11%) of affective psychosis, and 13 (7%) of delusional disorder and atypical psychosis (percentage males in non-schizophrenic psychoses: 52%).

Mean age of onset tended to be lower in the schizophrenic psychoses (16.0 years; SD = 2.6) compared with the other psychoses (17.2; SD = 2.7 in both other categories; $F = 2.7$; $p = 0.07$). Mean age of onset was 16.8 (SD = 2.5) in male subjects, and 15.5 (SD = 2.7) in females ($t = 3.4$; $p = 0.001$). Possible explanations for this discrepancy in age of onset have been discussed previously (Galdos et al., 1993a). There was no evidence that earlier age of onset in females was confined to any particular diagnostic category (ANOVA sex by diagnosis interaction: $F = 0.13$; $p = 0.9$).

The mean difference between actual age at admission and age at onset (henceforth called illness duration) was small at 0.49 years (SD 0.9 years); the median value was 0.0. There were no differences in illness duration between males and females ($t = 0.09$; $p = 0.9$) or diagnostic categories ($F = 0.5$; $p = 0.7$), nor was illness duration associated with age of onset ($r = 0.03$; $p = 0.7$).

3.2. Psychopathology in schizophrenic patients

In the first instance, analyses were confined to the group of schizophrenic patients only (Table 1). The likelihood of displaying delusional syndromes,

Table 1
Psychopathological syndromes and associations with sex and age of onset (age 11–21 years)

Psychopathological syndromes	Sex[a]	Age of onset[a]	Sex by age of onset interaction term	
	OR[b] 95% C.I.	OR[c] 95% C.I.	LRS[d]	p value
auditory hallucinations	1.3 (0.6–2.7)	1.3 (0.9–1.8)	4.9	0.03
passivity phenomena	1.0 (0.5–2.3)	1.2 (0.9–1.7)	3.9	0.05
thought interference	1.1 (0.5–2.2)	1.4 (1.0–1.9)	3.5	0.06
explanatory delusions	1.2 (0.5–2.8)	2.2 (1.5–3.1)	0.1	0.8
sexual delusions	3.6 (1.6–8.0)	1.2 (0.8–1.6)	0.7	0.4
delusions of reference	1.3 (0.6–2.6)	1.6 (1.2–2.2)	1.3	0.3
persecutory delusions	0.9 (0.4–1.9)	1.6 (1.2–2.2)	1.2	0.3
grandiose delusions	0.7 (0.3–1.6)	1.5 (1.0–2.1)	0.5	0.5
depressive delusions	0.8 (0.3–1.9)	1.2 (0.8–1.7)	0.02	0.9

[a] Sex and age of onset were entered together in the logistic regression equations; thus, the effect of each was examined while controlling for the other.
[b] OR = odds ratio; e.g. OR = 1.3 means females were 1.3-times more likely to have displayed the symptom.
[c] OR = odds ratio; e.g. OR = 1.3 means that with each unit in age of onset (5 consecutive age groups between ages 11–21) the odds of having the symptom increased with a factor 1.3.
[d] Likelihood ratio statistic on 1 df.

except depressive and sexual delusions, increased with age. Evidence of an association with gender was only present in sexual delusions, females more frequently displaying this symptom.

Evidence of significant interaction was present in typical schizophrenic symptoms such as auditory hallucinations, passivity phenomena, and thought interference. Subsequent stratified analysis revealed that there was a strong linear trend in the association with these symptoms in males, but not in females (Table 2).

3.3. The problem of diagnostic inaccuracy in adolescence

One of the problems in examining psychopathology in adolescence is the well known interchangeability between schizophrenic and affective features (Zeitlin, 1983), associated with unexpected responses to lithium in individuals diagnosed as schizophrenic (Horowitz, 1977). Furthermore, clinicians are not infrequently faced with 'atypical' presentations, that are not clearly schizophrenic,

Table 2
Association between first rank symptoms and age of onset, by sex

Age of onset	Auditory hallucinations		Passivity phenomena		Thought interference	
	Males	Females	Males	Females	Males	Females
11–12	0.04	[b]	0.00	8.0	0.0	2.0
13–14	0.24	1.38	0.14	2.4	0.22	0.86
15–16	0.16	0.90	0.61	3.2	0.38	2.0
17–18	0.27	1.0	0.63	4.0	0.60	0.0
19–21	1[a]	1[a]	1[a]	1[a]	1[a]	1[a]
Test for trend	$p=0.009$	$p=0.5$	$p=0.04$	$p=0.4$	$p=0.007$	$p=0.9$

[a] Baseline.
[b] Zero value in denominator: OR = infinite.

but nonetheless are associated with severe disability and requirement of long-term care (Steinberg, 1985). In view of the above factors, misdiagnosis is common, and especially in younger adolescents some time has to pass before the diagnosis can be established (Zeitlin, 1983; Steinberg, 1985; Werry, 1991). Therefore, we repeated the comparisons between adult and adolescent patients, using all patients with a diagnosis of functional psychosis. The results thus obtained were similar: significant associations were found between age of onset and the delusional syndromes, with the same exception of sexual delusions (significant association with gender) and depressive delusions (no association with either sex or age of onset). Again, significant sex by age of onset interactions in the same direction were apparent for hallucinations ($p=0.045$), passivity phenomena ($p=0.01$) and thought interference ($p=0.02$). In addition, sex by age of onset interactions approaching statistical significance now also became apparent for persecutory delusions ($p=0.07$) and delusions of reference ($p=0.08$). Stratified analysis for these also revealed a significant trend with increasing age in males (persecutory delusions: $p=0.001$; delusions of reference: $p=0.001$), but not in females (persecutory delusions: $p=0.6$; delusions of reference: $p=0.5$). A post-hoc stratified analysis in the schizophrenic category revealed a similar gender discrepancy for both persecutory delusions (males: $p=0.002$; females: $p=0.2$) and delusions of reference (males: $p=0.003$; females: $p=0.3$).

Although no significant gender by age of onset interactions could be demonstrated in the other delusional syndromes, a stronger age trend tended to be present in male patients. For example, the linear trend in the association between age of onset and presence of explanatory delusions was significant at the $p<0.001$ level in males, but at the $p=0.02$ level in females. However, no such discrepancy was detectable in depressive delusions, whereas in sexual delusions only an association with gender was apparent.

The findings in the combined diagnosis group were not the result of a 'confounding' effect of diagnosis, as the parameter estimates changed only by a trivial amount when diagnosis was controlled for in the regression equations.

4. Discussion

We found that, with the exception of sexual delusions and depressive delusions, the likelihood of displaying a range of delusional syndromes and typical schizophrenic experiences increased linearly with age from early adolescence to early adulthood. The association was stronger in males, especially for typical schizophrenic phenomena, where no age trend was apparent in females.

4.1. Methodological issues

Retrospective case-note studies are by definition suspect, as they rely on data collected by many different persons with different levels of experience. However, in our study, the most important case-note data were from the hand of psychiatric registrars belonging to the same rotational scheme, who had been trained to conduct the same semi-structured interviews (Institute of Psychiatry Training Committee, 1973). In the training scheme, there has been the same emphasis on positive symptoms, as defined by the PSE, over the period under investigation. Furthermore, if a systematic bias was operating in our data collection, this would be the same for early and later age of onset groups, as well as for males and females. It cannot, therefore, explain the fact that, for typical schizophrenic symptoms, age of onset differences were found in males, but not in females.

Substance misuse is unlikely to have played a role in this study, as only cannabis misuse is possibly sufficiently prevalent among patients in this part of South London to cause significant effects. Subjects with a toxic psychosis due to cannabis would have been excluded from the study, and for the drug to have a confounding effect on the reported associations, it would have to be strongly associated independently with psychopathology, age of onset and gender, which is unlikely.

As this was a sample of first admission cases, illness duration was on average brief (6 months), and not associated with either diagnostic category, age of onset, or gender. As actual age at admission corresponded closely to age of onset, the results are not obscured by the separate effects of actual age at admission and age of onset of psychosis.

We conclude that our findings cannot be explained away as artefactual, although we do not dispute the fact that additional data on intelligence and education would have improved the study (see below).

4.2. Interpretation of findings

It has been suggested that brain maturational processes around puberty are the anatomical substrate of the transition to the adult capacity for problem solving and abstract thinking (Feinberg, 1982/83, 1990; Goldman-Rakic, 1987). It is likely that the occurrence of positive symptoms of psychosis in adolescence is related to these maturational processes. The adolescent growth spurt begins in girls at about the age of 10.5, and in boys at about 12.5 years of age (Marshall and Tanner, 1986). Thus, the later manifestation of puberty and associated maturational processes in boys, could explain why typical schizophrenic ('first rank', Schneider, 1959) symptoms in early adolescence were relatively sparse, as seen in the more immature pattern of psychopathology of prepubertal psychosis, followed by an increase in the frequency of these symptoms through subsequent age of onset groups. In a previous publication (Galdos et al., 1993a), we provided epidemiologic evidence of a temporal relationship between puberty and the onset of psychotic symptoms, with girls showing an earlier onset than boys between the ages of 11–14 years, to be followed by a marked excess of boys among those with onset later in adolescence. The present results are compatible with an association between maturational processes in adolescence and the manifestation of symptoms of schizophrenia. Our findings concur with those of Bettes and Walker (1987), who showed a first significant increase in positive symptoms in girls between the ages of 9–10 and 11–12 years, whereas boys showed this increase between the ages of 11–12 and 13–14 years.

It is now well established that, even before the appearance of typical delusions and hallucinations, many schizophrenic patients display subtle behavioural, cognitive and motor developmental abnormalities when compared with their peers (Offord and Cross, 1969; Rutter, 1984; Aylward et al., 1984; Jones and Murray, 1993). This suggests that developmental events during adolescence interact with some pre-existing abnormality to produce psychotic symptoms (Weinberger, 1987; Murray et al., 1988), rather than an abnormality in the maturational process itself provoking these phenomena, as some authors have proposed (Feinberg, 1982/83; Saugstad, 1989).

Modern neuropsychological theories of schizophrenia have also considered developmental aspects of the formation of typical symptoms. For example, Frith (1994) discusses the work of Shultz and colleagues (1980), showing that in early childhood subjects could not distinguish between an intended movement of the lower leg and the reflexive movement initiated by a gentle tap of the knee. This suggests a lack of awareness of intentions, without which children cannot distinguish between intentional and accidental responses. It can be argued that development of intentional awareness is necessary in order to experience passivity phenomena, in that, although pathologically, experiences are recognized as not willed ('made'). Similarly, development of an awareness of the beliefs and intentions of others may be necessary for the formation of, for example, persecutory delusions, as they involve false inferences about the intentions of other people. Frith (1994) discusses experiments showing that in early childhood subjects cannot appreciate that others have false beliefs, and that more complicated tasks assessing beliefs in others cannot be achieved until late childhood.

In the delusional syndromes, it would appear that there is also a more straightforward relation with age, in that some delusions simply depend on age-specific knowledge. For example, explanatory delusions involving mechanisms such as X-rays and electricity require knowledge that depends on educational progress rather than on maturational processes per se. Such a general education effect may explain why, in our study, delusional syndromes showed a stronger age effect (effect of education), and less interaction with gender (indicating an association with biological maturation) than symptoms classically considered *experiences* rather than beliefs, such as auditory hallucinations, passivity phenomena and thought interference. For

example, a young patient might be able to explain that he *feels* controlled, without elaborating on commonly described mechanisms, such as electronic devices or telepathy. As these sort of explanatory delusions are arguably the most dependent on education, one would expect these to be strongly correlated with age. Our data support this notion, as explanatory delusions showed the strongest association with age, compared to the other psychopathological syndromes.

The fact that we were not able to formally examine associations with education, intelligence and verbal ability, all of which are relevant in this regard (Tsiantis et al., 1986), must be considered a limitation to our study. We feel that it is unlikely, however, that important differences in these variables would have existed between boys and girls.

Differences in age of onset are one of the most robust findings in schizophrenia research (Castle and Murray, 1991). A substantial proportion of schizophrenic patients display typical delusions and hallucinations before the age of 20; between the ages of 15 and 19 years, nearly twice as many boys than girls have the onset of the disorder (Galdos et al., 1993a). From our results it follows that differences in the psychopathology among male and female schizophrenics may be confounded by variation in the age of onset of the sample, if adolescent patients are included. Samples containing more early onset cases have a greater chance of finding gender differences (more positive symptoms in females) than samples with a later onset of illness. This may explain some of the inconsistencies in the literature on gender-related differences in the psychopathology of schizophrenia; some studies have reported an increased frequency of positive symptoms such as persecutory delusions in females (Goldstein and Link, 1988; Forrest and Hay, 1971), whilst others reported negative findings, or results in the opposite direction (Shtasel et al., 1992; McGlashan and Bardenstein, 1990). However, the issue of gender differences in the frequencies of specific 'first rank' symptoms (Schneider, 1959), such as passivity phenomena, was not addressed in these studies, and figures on the proportion of early onset cases are in general not available.

In conclusion, the comparative study of the psychopathology in psychotic patients from childhood through adulthood may shed light on the association between cerebral development and symptom expression, as well as on the underlying neuropsychological mechanisms of symptom formation. Gender differences in psychopathology may be confounded by the developmental modification of clinical presentation.

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