BY MARY ANN MOON

The use of cannabis at a younger age is associated with psychosis symptoms in early adulthood, according to a study published online in the Archives of General Psychiatry.

Such a link has been reported before, but this is the first study to demonstrate the association in a subgroup of sibling pairs, "thus reducing the likelihood that the association was due to unmeasured shared genetic and/or environmental influences," said Dr. John McGrath of the Queensland Brain Institute, Wacol, Australia, and his colleagues.

In addition, their study demonstrated a dose-response relationship between younger age at first marijuana use and higher risk of psychosis-related outcomes, they noted.

Earlier studies had found a link between early-onset cannabis use and later symptoms of psychosis, but there were "lingering concerns that the association may reflect methodological biases and unmeasured residual confounding" in those studies. Dr. McGrath and his associates examined the link using data from a birth cohort of more than 7,000 mother-infant pairs who were first studied in 1981-1984 and followed up 5, 14, and 21 years later.

A total of 3,801 of these infants and their close-in-age siblings comprised the subjects in this study. The latest follow-up occurred when they were aged 18-23 years. At that time, about 18% of the subjects said they had been using marijuana for 3 or fewer years; 16% said they had been using it for 4-5 years; and 14% said they had been using it for 6 or more years.

At this final follow-up, 65 of these subjects had received diagnoses of nonaffective psychosis because they met the criteria for schizophrenia (53 subjects), persistent delusional disorder (3), or acute transient psychotic disorders (9). An additional 233 subjects reported at least one visual or auditory hallucination on the Composite International Diagnostic Interview (CIDI).

Only subjects with the longest duration since first cannabis use—that is, those who started using marijuana at age 15 years or younger—were at significantly increased risk for developing symptoms of nonaffective psychosis in young adulthood.

Those who started using marijuana at that age were twice as likely to receive such a diagnosis than were subjects who said they had never used marijuana, the researchers said (Arch. Gen. Psychiatry 2010 [doi:10.1001/archgenpsychiatry. 2010.6]).

Compared with subjects who did not use cannabis, those who used it at a younger age were 4 times more likely to score in the top quartile on the 21-item Peters et al. Delusional Inventory (PDI) and to report hallucinations on the CIDI.

Moreover, the longer the interval since first cannabis use, the higher the risk of these adverse psychosis-related outcomes.

In a subsample of 218 sibling pairs,

there was a significant association between earlier first use of cannabis and higher scores on the PDI. For every additional year since first exposure to marijuana, the sibling with the younger age at first use scored one item higher than the other sibling, wrote the authors.

This study could delineate an association between early marijuana use and later symptoms of psychosis, and was not designed to determine causality. "We cannot confidently exclude the possibility that some of the cohort members may have developed psychosis as young adolescents, which may have contributed to subsequent [early] cannabis use," they added.

The National Health and Medical Research Council of Australia funded the study.

**Major Finding:** Those who started using marijuana at 15 were twice as likely to receive a diagnosis of nonaffective psychosis in young adulthood as their counterparts who said they never used.

**Data Source:** Prospective, sibling pair analysis of 3,081 adults born between 1981 and 1984.

**Disclosures:** None of the investigators had any financial conflicts of interest to report.

Adverse events in major depressive disorder (MDD): The most commonly observed adverse events associated with the use of paroxetine hydrochloride extended-release tablets were: abnormal ejaculation, abnormal vision, constipation, decreased libido, diarrhea, dizziness, female genital disorders, nausea, somnolence, sweating, trauma, tremor, and yawning. Adverse events in a study of elderly patients with MDD were: abnormal ejaculation, constipation, decreased appetite, dry mouth, impotence, infection, libido decreased, sweating, and tremor.

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