# Smoking Cessation Treatment for Patients With Schizophrenia

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*Objective: This study was an uncontrolled trial to assess the efficacy of a smoking cessation group program modified for individuals with schizophrenia. Method: Fifty outpatients with schizophrenia were divided into five groups who met separately for seven weekly sessions of a smoking cessation program. The subjects' schizophrenic and extrapyramidal symptoms were assessed before the group sessions began and after they had been completed. Assessments of smoking were made at those times and at 3-month and 6-month follow-ups. Results: Forty-two percent of the subjects had stopped smoking at the end of the group sessions; 16% remained abstinent at 3 months, and 12% at 6 months. These changes were statistically significant. There was no change in the positive or negative symptoms of schizophrenia. Conclusions: The results suggest that it is possible for individuals with schizophrenia to stop smoking.*
(Am J Psychiatry 1998; 155:974–976)

Individuals with schizophrenia smoke more than the general population and other psychiatric diagnostic groups (1, 2). In addition to the associated health hazards, the use of nicotine may interfere with the benefits of antipsychotic medication and increase side effects (2–4). Despite the increased focus on the health hazards of smoking, there are few reports of interventions for patients with schizophrenia (5, 6). A recent study (7) suggested that schizophrenic patients are interested in stopping smoking and are as motivated to do so as other people are. Unfortunately, the symptoms and cognitive and social deficits associated with schizophrenia make participation in existing smoking cessation programs difficult. Thus, the purpose of this study was to evaluate the effectiveness of a smoking cessation program modified for persons with schizophrenia.

## METHOD

The inclusion criteria for the study were that subjects be aged 18–65 years, be regular smokers, be stable outpatients, and meet the DSM-IV criteria for schizophrenia or schizoaffective disorder on the basis of a chart review. Persons who met the DSM-IV criteria for substance abuse or dependence (other than nicotine) were excluded. Sixty-five outpatients referred themselves to the study and completed the initial assessments. Fifteen had dropped out by the second group session.

Fifty subjects (29 male and 21 female) completed the group program and all four assessments. Their mean age was 40 years (SD=8), they had a mean of 12 years (SD=2) of education, and their mean number of previous hospital admissions was eight (SD=9). The majority were single, lived alone, and received government financial support. Twenty-eight subjects were taking typical antipsychotics, and 22 were taking atypical antipsychotics. The mean dose in chlorpromazine equivalents was 425.50 mg/day (range=20–1350). This was a relatively naive group of quitters: 30 subjects had made no previous attempt to quit, 17 had used nicotine replacement, and three had attended a smoking cessation program.

Two raters were trained on all measures, and adequate reliability was maintained. The Positive and Negative Syndrome Scale (8) and the Simpson-Angus Rating Scale for extrapyramidal effects (9) were administered before and after the group program. Two other scales were used at all assessments: the Fagerstrom Test for Nicotine Dependence (10) and the Reasons for Quitting Scale (11), a 20-item self-report scale that assesses four dimensions of motivation to quit smoking, namely, health concerns, self-control, immediate reinforcement, and social influence. At each assessment subjects were classified as smoking or abstinent at that point. Reports of abstinence were validated biochemically by determination of urinary cotinine levels. Cotinine has a half-life of 14 days, has been used to validate self-reports of not having smoked in the past 7 days, and may be useful up to 3–4 weeks for validation (12).

The subjects were given a complete description of the study, after which written informed consent was obtained. Assessments occurred before the group sessions began, after the group sessions ended, and 3 and 6 months after the last group session. The subjects were divided into five separate groups (N=12 for two; N=10, N=9, and N=7 for the other three) for the seven weekly group sessions, which lasted for 75 minutes. All sessions were led by a psychiatric nurse experienced in working with schizophrenic patients and in groups. She became a certified facilitator for smoking cessation by participating in a 1.5-day training workshop sponsored by the Alberta Lung Association. The cotherapist was a graduate student. The group treatment was based on the seven-session group program "Freedom From Smoking" designed by the American Lung Association and was modified to meet the needs of individuals with schizophrenia. Adherence to the modified program was monitored throughout and ranged from 94% to 98% for each of the seven sessions.

Presented at the 150th annual meeting of the American Psychiatric Association, San Diego, May 17–22, 1997. Received June 20, 1997; revisions received Oct. 10, 1997, and Jan. 20, 1998; accepted Jan. 30, 1998. From the Department of Psychiatry, University of Calgary. Address reprint requests to Dr. Jean Addington, Department of Psychiatry, Foothills Hospital, 1403 29th St., N.W., Calgary, Alta., Canada T2N 2T9; jmadding@acs.ucalgary.ca (e-mail).

Supported by a grant from the National Health, Research and Development Program of Canada.

**TABLE 1. Changes in Smoking and Symptoms of 50 Schizophrenic Patients in a Smoking Cessation Program**

| Variable | Before Group Program | | After Group Program | | 3-Month Follow-Up | | 6-Month Follow-Up | |
|---|---|---|---|---|---|---|---|---|
| | *N* | *%* | *N* | *%* | *N* | *%* | *N* | *%* |
| Patients who were nonsmokers[a] | 0 | 0 | 21 | 42*** | 8 | 16** | 6 | 12* |
| | *Mean* | *SD* | *Mean* | *SD* | | | | |
| Positive and Negative Syndrome Scale | | | | | | | | |
| Positive symptom score[b] | 11.27 | 4.4 | 11.37 | 4.6 | | | | |
| Negative symptom score[b] | 13.53 | 5.3 | 13.57 | 4.9 | | | | |
| Simpson-Angus Rating Scale score[b] | 2.71 | 2.6 | 3.18 | 3.3 | | | | |

[a]McNemar test for differences from pregroup measure.
[b]Paired t test; no significant difference between assessments.
*p≤0.03. **p=0.008. ***p<0.001.

The group program included positive reinforcement, learning and practicing alternative behaviors, and anxiety reduction strategies. There was a tolerance for positive symptoms, and social and financial limitations were considered. Teaching modifications were made to address neurocognitive deficits such as restricted information-processing capacity, memory and attentional difficulties, and poor executive functioning. A manual describing this group program in more detail is available from the first author.

Nicotine patches were offered to all subjects in conjunction with group attendance. Dosing began at 21 mg/day for 6 weeks and was then tapered to 14 mg/day and 7 mg/day for 2 weeks each.

## RESULTS

All reported results are for the 50 subjects who completed the group program. At the beginning of the program, the subjects were smoking an average of 28 cigarettes per day (SD=12) and had been smoking for an average of 23 years (SD=9). Nicotine dependence was high; the mean score was 6.39 (SD=2.09). Forty subjects initially used the nicotine patch. The average number of sessions attended was six; 50% of the subjects attended all seven sessions. According to the Reasons for Quitting Scale, the subjects were consistently more intrinsically than extrinsically motivated. Their degree of motivation did not differ from that reported in the literature for nonpsychiatric subjects (7, 11). In order of importance, reasons for quitting were health concerns, self-control, immediate reinforcement, and social influence. Changes over time were not significant.

Paired t tests revealed no changes in schizophrenic and extrapyramidal symptoms from before the group sessions to after (table 1). McNemar tests indicated that a significant number of the subjects (N=21) had quit smoking at the end of the group program. Although this number decreased at both the 3-month and 6-month follow-ups, the numbers were still significantly different from the pregroup assessment (table 1). All but one of the subjects who quit had used the nicotine patch.

We divided the subjects into four groups—those who never stopped smoking and those who were abstinent at the end of the group program, at 3-month follow-up, and at 6-month follow-up—and conducted analyses of variance to determine variables that might differentiate the groups. The results demonstrated no differences among any of the groups in medications, demographic characteristics, smoking variables, symptoms, or motivation. The one exception was attendance at the group sessions: the subjects who remained abstinent at the 3- and 6-month follow-ups attended all seven group sessions, those who had quit smoking at the end of the group program had attended 6.5 group sessions, and those who did not quit attended an average of 5.5 sessions ($F=6.12$, $df=3, 46$, $p=0.001$).

## DISCUSSION

Lack of a control group limits this study. However, the results were generally promising. These individuals had a long history of schizophrenia and had been heavy smokers for many years. All of the subjects expressed a strong desire to stop smoking, were intrinsically motivated, and generally showed good attendance. A substantial proportion of the subjects (42%) stopped smoking for at least 4 weeks. This number decreased to 16% at 3 months and to 12% at 6 months. Although these percentages are less than the 20%–25% rates for quitting in the general population (13), they are comparable to the 15% rate at 6 months reported by Ziedonis et al. (6). These results suggest that it is possible for individuals with schizophrenia to stop smoking; the difficult part is maintaining abstinence. Quitting smoking should not be considered an impossible task for individuals suffering from schizophrenia. A group approach with nicotine replacement and with modifications of the group sessions could be effective.

## REFERENCES

1. Hughes JR, Hatsukami DK, Mitchell JE, Dahlgran LA: Prevalence of smoking among psychiatric outpatients. Am J Psychiatry 1986; 143:993–997
2. Goff DC, Henderson DC, Amico E: Cigarette smoking in schizophrenia: relationship to psychopathology and medication side effects. Am J Psychiatry 1992; 149:1189–1194
3. Glassman AH: Cigarette smoking: implications for psychiatric illness. Am J Psychiatry 1993; 150:546–553
4. American Psychiatric Association: Practice Guideline for the

Treatment of Patients With Nicotine Dependence. Am J Psychiatry 1996; 153(Oct suppl)
5. Breckinridge J: Smoking by outpatients. Hosp Community Psychiatry 1990; 41:454–455
6. Ziedonis DM, Harris P, Wyatt SA, Trudeau K, George TP, Johnson D: Motivational enhancement therapy and nicotine replacement improve smoking cessation outcomes, in 1997 Annual Meeting Syllabus and Proceedings Summary. Washington, DC, American Psychiatric Association, 1997, p 101
7. Addington J, el-Guebaly N, Addington D, Hodgins D: Readiness to stop smoking in schizophrenia. Can J Psychiatry 1997; 42:49–52
8. Kay SR, Fiszbein A, Opler LA: The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. Schizophr Bull 1987; 13:261–276
9. Simpson GM, Amuso D, Blair JH, Farkas T: Phenothiazine-produced extrapyramidal system disturbance. Arch Gen Psychiatry 1964; 10:199–208
10. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom K: The Fagerstrom Test for Nicotine Dependence. Br J Addict 1991; 86: 1119–1127
11. Curry SJ, Wagner EH, Grothaus LC: Intrinsic and extrinsic motivation for smoking cessation. J Consult Clin Psychol 1990; 58: 310–316
12. Benowitz NL: The use of biologic fluid samples in assessing tobacco smoke consumption. NIDA Res Monogr 1983; 48:6–26
13. Lichtenstein E, Glasgow RE: Smoking cessation: what have we learned over the past decade? J Consult Clin Psychol 1992; 60: 518–527

# Inverse Relationship of Perinatal Complications and Eye Tracking Dysfunction in Relatives of Patients With Schizophrenia: Evidence for a Two-Factor Model

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*Objective:* *Because both smooth pursuit eye tracking dysfunction and obstetrical complications are significant risk factors for schizophrenia, the authors tested the predictions of a two-factor model of how eye tracking dysfunction and obstetrical complications covary in patients with schizophrenia, their siblings, and comparison subjects.* *Method:* *Psychiatric diagnoses, eye tracking dysfunction, and obstetrical complications noted in birth records were independently assessed in 18 patients with schizophrenia, 16 of their siblings without schizophrenia, and 49 comparison subjects with neither personal nor family histories of schizophrenia.* *Results:* *As hypothesized, 1) the combination of eye tracking dysfunction and perinatal obstetrical complications discriminated patients with schizophrenia significantly from subjects without schizophrenia, including siblings of patients with schizophrenia, and 2) eye tracking dysfunction and perinatal obstetrical complications manifested a significant inverse association in the nonschizophrenic siblings of patients with schizophrenia.* *Conclusions:* *These results support a two-factor model in which obstetrical complications often interact with genetic liability, indicated by eye tracking dysfunction, to produce schizophrenia.*
(Am J Psychiatry 1998; 155:976–978)

The prevalence of dysfunction in smooth pursuit eye tracking is significantly elevated in patients with schizophrenia and their relatives, including monozygotic co-twins (1–3). Genetic modeling of data from the families of patients with schizophrenia suggests that eye tracking dysfunction is a sensitive behavioral indicator of an autosomal dominant gene that markedly increases the risk for schizophrenia (4). The model suggests that approximately 53% of gene carriers have eye tracking dysfunction, whereas less than 10% develop schizophrenia. Rates of obstetrical complications, particularly perinatal ones, are also higher in patients with schizophrenia than in comparison subjects (5, 6), including siblings of patients with schizophrenia (6) and monozygotic co-twins.

A two-factor model of schizophrenia is suggested by

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Supported by NIMH grants MH-31154, MH-49487, MH-31340, and MH-01021.
The authors thank Steven Matthysse, Ph.D., for advice and Rebecca Bloom, Clara Lajonchere, Christian LaVancher, and David Medoff for assistance.

inverse associations between neurological signs and psychopathology found in the nonschizophrenic relatives of patients with schizophrenia (7). This model proposes that two major etiologic factors run in the families of patients with schizophrenia, and increase the risk for schizophrenia markedly when they occur together, but are statistically independent of each other in the general population.

This model predicts that, although patients with schizophrenia have elevated levels of each risk factor, the joint presence of these two factors discriminates patients with schizophrenia particularly well from subjects without schizophrenia, including relatives of patients with schizophrenia. More important, it predicts that nonschizophrenic relatives of patients with schizophrenia will have significantly higher rates of individuals with one or the other—but not both—risk factors (7). Because the two risk factors are distributed independently, measures associated with one or the other underlying risk factor will be inversely related among subjects without schizophrenia, particularly in relatives of patients with schizophrenia; Matthysse provided a mathematical proof that this is a logical corollary of the model (8).

Findings on perinatal obstetrical complications and Trail Making, a neuropsychological measure, fit the model well: the combination of perinatal obstetrical complications and poor Trail Making performance significantly discriminated patients with schizophrenia from subjects without schizophrenia, and poor Trail Making and perinatal obstetrical complications were significantly and inversely related among the nonschizophrenic siblings of patients with schizophrenia (8). Complementary research (5) found that the adult offspring of patients with schizophrenia had fewer obstetrical complications if the offspring were diagnosed as having borderline schizophrenia rather than psychiatrically normal, as expected if obstetrical complications often interact with genetic liability to produce schizophrenia (9).

Eye tracking dysfunction is of particular interest for the two-factor model because research suggests that eye tracking dysfunction indexes genetic liability for schizophrenia (1–4). We hypothesized that 1) the combination of eye tracking dysfunction and perinatal obstetrical complications discriminates patients with schizophrenia significantly from subjects without schizophrenia, including relatives of patients with schizophrenia, and 2) eye tracking dysfunction and obstetrical complications are inversely related among subjects without schizophrenia, particularly siblings of patients with schizophrenia.

## METHOD

Probands with schizophrenia and mood disorders were recruited from patients consecutively admitted to state and private inpatient psychiatric hospitals. Diagnoses were made by experienced investigators who were blind to obstetrical and eye tracking data and who used DSM-III or DSM-III-R criteria as well as information from chart reviews, family informants, and, for most subjects, structured interviews. Written informed consent was obtained from all study participants after study procedures were fully explained. Data on eye tracking dysfunction, diagnosis, and obstetrical complications were available for 83 adults: 18 patients with schizophrenia, 16 of their nonschizophrenic siblings from nine families, and 49 comparison subjects with no personal or family history of schizophrenia. Comparison subjects included 26 normal subjects (normal probands and their well relatives) and 23 others, including four probands with major depression, three psychiatrically ill relatives of comparison probands, and 16 first-degree relatives of probands with bipolar disorder or major depression.

Mean ages and male-female ratios were 29.0 years (SD=5.8) and 16:2 for patients with schizophrenia, 32.1 years (SD=7.9) and 8:8 for the siblings of patients with schizophrenia, and 26.5 years (SD=7.2) and 22:27 for all other subjects. All subjects were born in the United States and, except for three African American comparison subjects, all were Caucasian. Mean illness duration for patients with schizophrenia was 6.2 years (SD=3.7).

Procedures for recording eye tracking dysfunction were standard ones used in eye tracking studies and are described elsewhere (2, 4). Eye tracking records were blindly reviewed by two independent raters, who assigned qualitative scores of normal or abnormal. Obstetrical data in maternity hospital records on subjects' gestations and births were scored blind to diagnostic and eye tracking dysfunction data; the raters applied published scales developed by an eminent obstetrician and used in studies by various investigators (e.g., references 5 and 6). The scale generated a summary score for each subject that was the algebraic sum of all labor and delivery complications present, with more severe complications weighted more heavily. Scoring with these scales yields satisfactory interrater agreement in our laboratory (6). Spearman rank-order correlations (and two-tailed tests) were used to investigate relations between eye tracking dysfunction and obstetrical complication scores, which are ordinal data.

## RESULTS

The combination of eye tracking dysfunction and a higher perinatal obstetrical complication score (rating of 3.00 or greater, corresponding to more than one or two mild complications) occurred in 22% (N=4) of patients with schizophrenia but only 1.5% (one normal comparison subject) of 65 subjects without schizophrenia, who included 20 subjects with nonschizophrenic disorders (p=0.006, Fisher's exact test). Mean obstetrical complication scores were 3.00 (SD=2.95) for patients with schizophrenia and 1.75 (SD=1.53) for the 16 siblings—but only 0.50 (SD=0.84) for the six siblings with eye tracking dysfunction—and 2.16 (SD=2.04) for all 49 comparison subjects, including 2.46 (SD=2.32) for 26 normal comparison subjects and 1.83 (SD=1.67) for the 23 other comparison subjects.

Spearman correlations between eye tracking dysfunction and perinatal obstetrical complication scores were, respectively, $r_s$=–0.07 (n.s., N=18) for patients with schizophrenia, $r_s$=–0.22 ($p<0.05$, N=65) for all subjects without schizophrenia, and $r_s$=–0.66 (p=0.005, 95% confidence interval=–0.24 to –0.87, N=16) for the nonschizophrenic siblings of patients with schizophrenia. These correlations did not reflect demographic variables, which were not significantly correlated with eye tracking dysfunction or obstetrical complications.

## DISCUSSION

The combination of eye tracking dysfunction and a high perinatal obstetrical complication score significantly discriminated patients with schizophrenia from subjects

without schizophrenia, including siblings of patients with schizophrenia. Moreover, eye tracking dysfunction and perinatal obstetrical complications were significantly and negatively correlated among the nonschizophrenic siblings of patients with schizophrenia—a distinctive prediction of the two-factor model of schizophrenia.

These results complement evidence for a two-factor model from research on patients with schizophrenia involving other variables, including neurological signs (7) and neuropsychological deficits (8, 10). The findings are thus theoretically intriguing but need replication.

REFERENCES

1. Holzman PS, Matthysse S: The genetics of schizophrenia: a review. Psychol Sci 1990; 1:279–286
2. Levy DL, Holzman PS, Matthysse S, Mendell NR: Eye-tracking and schizophrenia: a selective review. Schizophr Bull 1994; 20: 47–62
3. Iacono WG, Moreau M, Beiser M, Fleming JAE, Lin RY: Smooth-pursuit eye tracking in first-episode psychotic patients and their relatives. J Abnorm Psychol 1992; 101:104–116
4. Matthysse S, Holzman PS, Lange K: The genetic transmission of schizophrenia: application of Mendelian latent structure analysis to eye tracking dysfunction in schizophrenia and affective disorders. J Psychiatr Res 1986; 20:57–76
5. Parnas J, Schulsinger F, Teasdale TW, Schulsinger H, Feldman PM, Mednick SA: Perinatal complications and clinical outcome within the schizophrenia spectrum. Br J Psychiatry 1982; 140: 416–420
6. Kinney DK, Levy DL, Yurgelun-Todd DA, Medoff D, Lajonchere CM, Radford-Paregol M: Season of birth and obstetrical complications in schizophrenics. J Psychiatr Res 1994; 28:499–509
7. Kinney DK, Yurgelun-Todd DA, Woods BT: Hard neurologic signs and psychopathology in relatives of schizophrenic patients. Psychiatry Res 1991; 39:45–53
8. Kinney DK, Yurgelun-Todd DA, Waternaux C, Matthysse S: Obstetrical complications and trailmaking deficits discriminate schizophrenics from unaffected siblings and controls. Schizophr Res 1994; 12:63–73
9. Mednick SA: Breakdown in individuals at high risk for schizophrenia: possible predispositional perinatal factors. Ment Hyg 1970; 54:50–63
10. Yurgelun-Todd DA, Kinney DK: Patterns of neuropsychological deficits discriminate schizophrenics from siblings and controls. J Neuropsychiatry Clin Neurosci 1993; 5:294–300