Smoking and schizophrenia: understanding the association, and focussing treatments

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- Strong association between smoking and mental illness
- People with mental illness consume half of all cigarettes
- Little or no impact from public health messages
- Rates of smoking in people with schizophrenia 70-90%
- Very low motivation to quit
- Low rates of actual quitting
Why such high rates?

- Positive reinforcement:
  - Reward (DA mediated)
  - Decrease anxiety, depression
  - Ameliorate akathisia

- Negative reinforcement:
  - Ameliorate cognitive dysfunction
  - “Incentive salience” ie. craving
  - Mediated by DA in orbitofrontal cortex and insula (pts with insula stroke stop smoking!)
Psychosocial issues

- Boredom
- Social affiliation
- Institutional ethos
- Peer pressure
- Staff factors?!
100 smokers with schizophrenia compared with 100 non-schizophrenia smokers

All had a cigarette before testing!

Schizophrenia patients:

- Lower on Fagerstrom Dependency Index (4.7 vs. 5.3; $p=0.08$)
- No different on Tobacco Craving Questionnaire immediately post-cigarette (46.7 vs. 42.8; $p=0.15$) but *much higher at 15 min* (50.0 vs. 38.6; $p=0.001$)
- Lower reported withdrawal effects at 24 hours abstinent
- Smoking Consequences Questionnaire (SCQ-A): schizophrenia patients reported greater benefits from smoking, including taste/sensorimotor, negative feeling reduction, state enhancement

- Reasons for Quitting Scale (RFQ): more likely to consider quitting due to social pressure; less likely due to health concerns, immediate reinforcement

- Lower appreciation of health consequences

- Lower on stages of change (75% pre-contemplation vs. 62% in non-schizophrenia sample)
Zebrafish: nicotine enhances learning and reduces “anxiety”

Rats: fear conditioning paradigm (footshock):
- Nicotine acutely enhances hippocampal-dependent learning
- Nicotine withdrawal reverses these effects
- Varenicline (partial agonist) restores learning
Animal (rat) model of schizophrenia (hippocampal ‘developmental’ lesion):

- Respond better than un-lesioned rats to cognitive enhancement effects of nicotine
Neurocognitive deficits in schizophrenia (e.g., attention, memory, verbal learning, spatial working memory) can be ameliorated to some degree by nicotine.

Conversely, nicotine withdrawal worsens these deficits.

Nicotine can reverse P-50 evoked potential deficits in schizophrenia.
Addressing smoking in people with schizophrenia
The Healthy Lifestyles Project:
Pilot Data from a Multi-component Risk Factor Intervention for People With Severe Mental Illness

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Aims of the Project (1)

- Assess the feasibility of conducting a multi-component risk factor intervention to promote smoking cessation and change in body mass index (BMI) among people with psychosis.

- Determine if a reduction in smoking and weight is associated with improved body image, ↓ depression and ↑ quality and enjoyment of life.
Simply: result in change in participant’s lifestyle, and cardiovascular risk factors in terms of 3 main areas:

1. Smoking
2. Diet
3. Level of Physical Activity
Target Group

- People aged 18-60 with a diagnosis of psychosis
- Current cigarette smoker
- Body Mass Index (BMI) of >30
- Informed consent
- Willing to attempt to make some change in their smoking, diet, and level of physical activity
Study Design

- Informed Consent
- Baseline Assessment
- Intervention program for 11 weeks
- Second assessment at 3 months by an independent rater
Assessments

- Demographic details
- Physical measures
- Smoking and Drug use History
- Dietary Record
- Physical Activity Log
- Test for Nicotine Dependence
- Carbon Monoxide Reading
- Reasons for Smoking/Quitting
Assessments

- Readiness and Motivation to Change
- Diagnosis
- Levels of psychosis and depression
- Medication
- Quality of Life
- Nicotine Withdrawal Symptoms
- Side-effects rating scale
Assessments of Cardiovascular Risk Factors

- **Baker Heart Research Institute**
  - Prof Garry Jennings; Prof Simon Stewart; Jan Jennings

- **Overall Coronary Risk Percentile**
  - Blood pressure, cholesterol, smoking
  - Age and gender
  - 50 average
  - > 80 highest risk
The Intervention

- Weekly sessions for 7 weeks
- Two booster sessions (Week 9 and Week 11)
- Nicotine Replacement Therapy (NRT): Nicabate CQ patches and Lozenges
  - Step 1: 21mg patch for 6 weeks
  - Step 2: 14mg patch for 2 weeks
  - Step 3: 7mg patch for 2 weeks
The Intervention

- Cognitive Behaviour Therapy (CBT)
  - Motivational Interviewing

- Provision of Education:
  - Smoking and smoking cessation
  - Diet
  - Physical activity

- Resources:
  - Pedometer
  - Information sheets/handouts
Results

- Four sites: 43 participants
- Treatment sessions:
  - < 5 sessions = 5 (11.6%)
  - 5-8 sessions = 2 (4.7%)
  - All 9 sessions = 36 (83.7%)
- Follow-up assessment:
  - 43 participants (100%!)
Sample Details

- 43 participants
- Mean age: 36 years
- 58% male
- Most common diagnoses:
  - Schizophrenia (54%)
  - Schizoaffective disorder (26%)
Smoking Results

- A significant decrease in the number of cigarettes smoked over time
  - 30.8 cig/day to 17.2 cig/day, \( p = .000 \)

- Smoking status:
  - No change or increase = 16%
  - Less than 50% reduction = 35%
  - 50% reduction or more = 49%

- No cigarettes in past week = 19%

- Not a single cigarette since QUIT date = 12%
Weight Results

- Non-significant decrease in weight over time
  - 101kg to 99kg, $p = .014$

- Non-significant decrease in BMI over time

- Weight status:
  - No change or weight gain = 46%
  - Up to 5% reduction in body weight = 33%
  - More than 5% reduction in body weight = 21%

- Significant improvement in Quality of Life related to weight over time
Exercise Results

- Almost significant increase in number of exercise sessions per week over time
  - 3.3 times to 4.8 times/week, $p = .003$

- Significant increase in the frequency of moderate exercise sessions over time
  - 2.4 times to 3.4 times/week, $p = .001$
Cardiovascular Risk Results

- **Significant** decrease in Overall Coronary Risk Percentile over time
  - 74 to 64, \( p = .001 \)

- Fewer participants with an Overall Coronary Risk Percentile > 80 at follow-up:
  - 55% vs 42%
Limitations of the Study

- Duration of treatment
- No control group
- Resources and time
Varenicline & Smoking Cessation
Varenicline

- Partial agonist at nicotinic α4β2 receptor
- Low to moderate levels of dopamine release
- Reduces rewarding & reinforcing effects of smoking
- 12 week course with counselling
- Meta-analysis vs NRT
  - $3/12$: OR 1.78 (1.23 - 2.57)
  - $12/12$: OR 1.66 (1.17 - 2.36)
- RCT vs bupropion & placebo (n = 1025)
  - more effective than bupropion for smoking cessation (OR 1.93 (1.40 - 2.68))
- RCT of maintenance therapy
  - greater abstinence rates (OR 1.34 (1.06 - 1.69))
Meta-analysis

Varenicline 2.0mg/d produced highest odds ratio for quitting of 3.1; abstinence rate 33.2%

Reducing the dose to 1.0mg/d reduces abstinence rate to 25.4%
Three most common adverse events

- Nasopharyngitis (35.9% versus 38.3%)
- Nausea (24.4% versus 7.8%)
- Headache (10.3% versus 2.6%)
Psychiatric side effects (preclinical studies)

"infrequent"
- agitation
- aggression
- mood swings

"rare"
- euphoria
- psychosis
Psychiatric Effects (2)

- FDA advisory (MedWatch)

**days to weeks after commencing:**

- erratic behaviour
- depression
- agitation
- suicidal ideation
- suicide attempts
- completed suicide
Use in People with a Mental Illness

- **Stapleton et al (2007)**
  - pre - post-comparison of outcomes with NRT, then Varenicline
  - few mentally ill patients (only 7 (0.2%) had psychosis)

- **Freedman (2007)**
  - case report of worsening psychosis in schizophrenia patient

- **Kohen & Kremen (2007)**
  - case report of mania in bipolar patient

- **Pumariega et al (2008)**
  - case report of mania in patient with past depression and family history of bipolar
Current Study

- 12 week open trial of CBT + Varenicline in patients with psychosis

- Assessments (baseline, 12 weeks & 24 weeks)
  - Tobacco Use:
    - Opiate Treatment Index
  - Readiness & Motivation to Quitt
  - Fagerstrom test for Nicotine Dependence
  - CO levels - Smokerlyser
Current Study

Psychiatric:
- BPRS
- BDI
- YMRS

Functioning:
- GAF
- SF36

Side effects:
- standardised questionnaire
Added Safety Parameters

- Only experienced staff to conduct intervention and assessments

- BDI & MADRS & VBPTS
  - day 3 and at every session

- Phone call check between every session
<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnoses</th>
<th>Cigs at Entry</th>
<th>Cigs at 3 mths</th>
<th>Cigs at 6 mths</th>
<th>Side Effects/Problems</th>
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<td>Mood disorder with psychotic</td>
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<td>Poor concentration, increased appetite, abnormal dreams, transient depression</td>
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<td>Dry mouth, Nausea,Sweating</td>
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<td>0</td>
<td>Constipation, headache, abnormal dreams (but liked them!)</td>
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<td>Cigs at 3 mths</td>
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