What do we know about treatment-resistant schizophrenia? A systematic review

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Background:
Schizophrenia is the most common severe psychotic disorder and a major public health problem. It begins in early adult life and afflicts about 1% of humans, in Northern Finland even 1.8% of population. Treatment-resistant schizophrenia (TRS) is a severe form of schizophrenia. One of fifth to one of third of all patients with schizophrenia are resistant to treatment. Treatment resistance can be diagnosed after at least two failed trials of different antipsychotics with adequate dose and length of treatment.

Objective:
To do a systematic review of the current literature on TRS, to determine the knowledge on TRS and to find out the extent and the quality of research on TRS.

Methods:
Studies were systematically collected using the databases of PubMed, Scopus and CINAHL, by using the following search strategy as a title search: (“ultra-resistant” OR “treatment-refractory” OR "treatment-resistant") AND schizophrenia AND "English"[Language]. The articles met the following criteria; English language and an original study or a review on TRS.

Results:
The literature search located 403 studies. After abstract and title review, 259 studies were included and the studies were categorized by topic (Table 1.). Most of the studies considered medication and there were only few studies on treatment, prognosis or neurobiology of TRS. Definitions of TRS varied notably and in most of the non-pharmacological studies the samples were fairly small. Regarding treatments, clozapine, ECT and cognitive-behavioral therapy have shown effectiveness, though the quality of the research on interventions is limited. Very little is known about risk factors of TRS and predictors of outcome in TRS.

Conclusions:
There is a lack of studies on epidemiology, for example risk factors of TRS, as well as outcomes and longitudinal course. The number and quality of studies on medications of TRS are surprisingly low. Our findings suggest TRS is poorly studied and understood condition, contrasted to its high prevalence, clinical importance and poor prognosis.

Table 1. Studies on TRS categorized by topic

<table>
<thead>
<tr>
<th>Topic</th>
<th>Total number of studies</th>
<th>Original articles</th>
<th>Reviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition of TRS</td>
<td>12</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Psychotherapy in TRS</td>
<td>12</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>ECT and rTMS in TRS</td>
<td>15</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Prognosis of TRS</td>
<td>15</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Brain structures and functioning in TRS</td>
<td>10</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Cognition in TRS</td>
<td>7</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Genetics and TRS</td>
<td>15</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Other studies in neurobiology of TRS</td>
<td>15</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Other, miscellaneous studies on TRS</td>
<td>5</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Studies on medication</td>
<td>153</td>
<td>108</td>
<td>45</td>
</tr>
</tbody>
</table>

TRS = Treatment-Resistant Schizophrenia, ECT = Electroconvulsive therapy, rTMS = Repetitive Transcranial Magnetic Stimulation

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Mobile Therapeutic Attention for Patients with Treatment-Resistant Schizophrenia

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