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SCHIZOPHRENIA Factsheet

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What are first and second generation antipsychotics?

First generation 'typical' antipsychotics are an older class of antipsychotic than second generation 'atypical' antipsychotics. First generation antipsychotics are used primarily to treat positive symptoms such as hallucinations and delusions. Second generation antipsychotics are also effective for the positive symptoms of schizophrenia, and it is sometimes claimed that they are more effective than first generation antipsychotics in treating the negative symptoms of schizophrenia. Negative symptoms include a lack of ordinary mental activities such as emotional expression, social engagement, thinking and motivation. High potency first generation antipsychotics usually have high affinity for the dopamine receptor and therefore induce extrapyramidal side effects by the blockade of these dopamine receptors. Extrapyramidal side effects include dyskinesias (repetitive, involuntary, and purposeless body or facial movements), Parkinsonism (cogwheel muscle rigidity, pill-rolling tremor and reduced or slowed movements); akathisia (motor restlessness, especially in the legs, and resembling agitation), and dystonias (muscle contractions causing unusual twisting of parts of the body, most often in the neck). Second generation antipsychotics generally have a lower affinity for the dopamine receptor and also block serotonin receptors, so may be associated with lower risk of these side effects.

What is the evidence for first versus second generation antipsychotics?

Efficacy

Moderate to high quality evidence suggests a small effect of improved overall symptoms with second generation antipsychotics, particularly olanzapine, amilsulpride, and risperidone, compared to first generation antipsychotics, particularly high-dose haloperidol (>12mg/day), which is not as effective as lower doses. There is a small effect of less all-cause study discontinuation with olanzapine, risperidone, or amisulpride compared to haloperidol in the short-term. Moderate quality evidence suggests only olanzapine may result in less long-term discontinuation due to drug intolerability or inefficiency. Moderate to high quality evidence suggests olanzapine and risperidone may improve cognition more effectively than haloperidol, and moderate quality evidence suggests amisulpride, clozapine and sertindole may improve quality of life more effectively than first generation antipsychotics in general.

Side effects

Moderate quality evidence suggests a medium-sized effect of less extrapyramidal side effects with second generation antipsychotics, particularly olanzapine and risperadone, than with haloperidol. Clozapine, olanzapine, and risperidone may also produce fewer extrapyramidal side effects when compared to low-potency first generation antipsychotics. Moderate quality evidence suggests clozapine, quetiapine, and zotepine may be more sedating, and aripiprazole less sedating, than haloperidol. Compared with low-potency first generation antipsychotics, only clozapine may be more sedating. Moderate to high quality evidence suggests less use of benzodiazapines, anticholinergeric medications, and beta-blockers with olanzapine than with haloperidol. Moderate quality evidence suggests amisulpride, clozapine, olanzapine, quetiapine, risperidone, sertindole, and zotepine may be associated with more weight gain than haloperidol, with no differences when compared to low-potency first generation antipsychotics. Moderate quality evidence suggests more cholesterol change with olanzapine than haloperidol, and more tryglyceride change with amisulpride than haloperidol.

For more information see the technical table

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NeuRA (Neuroscience Research Australia) is one of the largest independent medical and clinical research institutes in Australia and an international leader in neurological research.

Diseases of the brain and nervous system pose the greatest health, economic and social burden of any disease group because they are chronic, debilitating and have no known cures.

Medical research is the cornerstone of efforts to advance the health and wellbeing of families and the community. Our dedicated scientists are focussed on transforming their research into significant and practical benefits for all patients.

While we hope you find this information useful, it is always important to discuss any questions about schizophrenia or its treatment with your doctor or other health care provider.

HOW YOUR SUPPORT HELPS

We are able to make significant advances due to the generosity of countless people. Your donation allows us to continue to work towards transforming lives. For information on how you can support our research, phone **1300 888 019** or make a secure donation at **neura.edu.au/donate/schizophrenia**.

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