

# The Effects of Modafinil in People with a Diagnosis of Schizophrenia

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## Abstract

This review seeks to describe the use and effects of the drug modafinil. Specifically, it presents the research of the impact of modafinil for people with diagnosis and experience of schizophrenia. Recent reviews have shown that modafinil can positively impact on cognitive function in people with a diagnosis of schizophrenia. There is emerging evidence for the positive impact of modafinil on negative symptoms, functioning, quality of life, wellbeing, and body mass index (BMI) for people with schizophrenia. Compared to other central nerve stimulant (CNS) drugs, modafinil has a low risk of dependency and few negative side effects; but there are risks of triggering positive symptoms in schizophrenia. A well designed and sufficiently large randomised control trial is required to test the potential of the impact of modafinil in the lives of people with a diagnosis of schizophrenia. Future research should report participant's perspective of the value of modafinil connected to what concerns them and what they want to achieve in their lives.

## Keywords

Modafinil, Cognitive Enhancement, Schizophrenia, Quality of Life, Wellbeing, Recovery

## 1. Introduction

Modafinil is a central nerve stimulant (CNS) eugeroic that directly increases cortical catecholamine levels, indirectly upregulates cerebral serotonin, glutamate, orexin, and histamine levels, and indirectly decreases cerebral gamma-aminobutyric acid levels [1]. It is prescribed as a wakefulness enhancer; in narcoleptic patients it is an effective treatment of excessive daytime tiredness [2]. Modafinil is indicated for the treatment of excessive sleepiness in adults with narcolepsy, with or

without cataplexy [3] and may be considered for excessive daytime sleepiness in people with Parkinson's disease [4]. Unlike other CNS drugs, modafinil has a low potential for dependence [3] [5] and has low side effect profile [3].

In healthy non-sleep deprived individuals modafinil can enhance attention, executive functions, and learning; and there is a low level of side effects or mood changes [1]. Modafinil can enhance task enjoyment and performance on cognitive tests of planning and working memory in healthy non-sleep deprived individuals [6]. Modafinil can also maintain wakefulness, memory and executive functions in sleep deprived healthy individuals [7].

## 2. Schizophrenia

For many people with a diagnosis of schizophrenia antipsychotic agents have reduced the disease burden and disability caused by positive symptoms (e.g. delusions and hallucinations) [8], but they have limited effect in managing negative symptoms [9]. However, negative symptoms (e.g. affective flattening, avolition, asociality, anhedonia, cognitive impairment and functional issues related to cognitive impairment) due to the disease and sedative side effects of antipsychotic agents remain an issue for many [10]. Evidence indicates that negative symptoms contribute more to impaired quality of life and poor functioning than positive symptoms [9]. These factors can negatively impact on engagement in therapy and recovery.

Cognitive impairment is a core feature of schizophrenia, it persists during symptomatic remissions and cognitive impairment can predict functional outcome in chronic schizophrenia [11]. In schizophrenia processing speed in performance intelligence and fluid intelligence is impaired, negatively impacting on functioning required for adaptive behaviour [12]. Arguments have been made of the importance of considering schizophrenia, from the perspective of treatment, as a cognitive illness [13].

## 3. Modafinil and Schizophrenia

A systematic review of the effects of modafinil on cognition and emotion in schizophrenia found that modafinil improves cognitive functions, with pro-mnemonic effects and problem-solving improvements, and enhances emotional processing [14]. Reviewing evidence reported subsequent to this review supports these findings [15]. Evidence reviews have concluded that improvement in cognitive functions induced by modafinil could have a beneficial effect on broader aspects of patients' lives, including functional outcomes, quality of life and wellbeing [14]. In studies which employed neuroimaging, modafinil produced an increased activation of the anterior cingulate cortex and dorsolateral prefrontal cortex [16] [17].

Modafinil has been found to enhance subjective wellbeing and nurse rated therapeutic change (cooperation, irritability, manifest psychosis, personal neatness, psychotic depression, social competence and social Interest) in people with

schizophrenia [18]. However, these findings were based on a small RCT (14 participants given modafinil and 6 placebo).

A systematic review of the effects of modafinil on the negative symptoms of schizophrenia found that modafinil reduces negative symptoms for some cohorts of people with schizophrenia [19]. The review also reported that modafinil is safe, well tolerated and does not worsen other symptom dimensions [19]. Furthermore, a placebo controlled RCT found that modafinil was effective in reducing deficits in inhibitory control [20].

The Positive and Negative Syndrome Scale (PANSS) [21] is a widely used measure of positive and negative symptoms. A study reported that modafinil produced significant positive effect on PANSS total and negative scores [22]. However, in this study participant numbers were low (23 drug v. 23 placebo) and the researchers concluded that larger controlled trials are needed before recommendation for a broad clinical application can be made. A systematic review of psychostimulants to treat negative symptoms of schizophrenia concluded that large controlled trials to characterise the effects of psychostimulants in clearly defined schizophrenia patient groups are required [23].

There are other potential positive effects of modafinil. One small (12 drug v. 12 placebo) RCT found improved parkinsonian symptoms in schizophrenia or schizoaffective disorder [24]. Furthermore, through a reduction in appetite modafinil has been found to reduce food intake in healthy people [25] [26] and may counteract the weight gain caused by anti-psychotics [27] which increase appetite [28]. However, modafinil is not without risks when used with people with a diagnosis of schizophrenia, there have been reported cases of increased positive symptoms [29].

#### 4. Considerations for Clinical Use

Medium or long stay in-patients with schizophrenia may be “stuck in the system” because they cannot engage in therapy and so struggle to make progress towards successful community based life. This is true for people who are in secure and non-secure facilities. For those in secure facilities, if they cannot engage in therapy related to offending this may block progress to lower level security and possible release to the community. Possible modafinil enhanced cognitive function and reduced negative symptoms may enable engagement in therapy to allow progress.

Modafinil is not licensed as adjunctive therapy in people with schizophrenia. There has been insufficient consistent evidence on which to base a recommendation for modafinil as adjunctive therapy in schizophrenia [30], but the evidence for its value has been growing [15]. Clinicians can prescribe modafinil “off label” as a treatment in people with a diagnosis of schizophrenia, but there is little evidence that this is happening. This is a situation that may change as more evidence emerges for the value of modafinil and people seek solutions to address cognitive issues associated with the experience of schizophrenia, but prescribing clinicians need to consider potential risks [29].

## 5. Conclusions

Research has shown that modafinil can enhance cognitive function in schizophrenia [14] [15] and has potential to enhance real life functioning [16] and reduce negative symptoms [17]. This potential requires further research. A well designed and sufficiently powered RCT is required to assess the impact of modafinil on the lives of people with medium and long-term experience of schizophrenia. This research would address whether modafinil improves recovery, wellbeing, negative symptoms of schizophrenia, psychopathology, progress in therapy, and body mass index; and whether any improvements are sustained beyond the period of prescription.

This research would ask: “what is the value of modafinil in the lives of people with long term experience of schizophrenia, and does this outweigh risks?” and therefore: “should it be prescribed?” It would also seek to find out which people may benefit: what are the characteristics of those who benefit from taking modafinil. Perhaps most importantly it would seek to find out participants perspectives of the value of modafinil connected to what concerns them and what they want to achieve. The research would seek to ask: “what changes did you observe?”, “did it enhance your quality of life and wellbeing?” and “would you recommend a course of modafinil to people with medium to long term experience of schizophrenia?”

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### Abbreviations Note List

BMI—Body Mass Index  
CNS—Central Nerve Stimulant  
PANSS—Positive and Negative Syndrome Scale  
RCT—Randomised Control Trial