

Paper 2

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COGNITIVE-BEHAVIOURAL THERAPY V. MIRTAZAPINE  
FOR CHRONIC FATIGUE AND NEURASTHENIA:  
A RANDOMISED PLACEBO-CONTROLLED TRIAL

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## Cognitive-behavioural therapy v. mirtazapine for chronic fatigue and neurasthenia: randomised placebo-controlled trial

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### Abstract

#### Background

Single interventions in chronic fatigue syndrome have shown only limited effectiveness, with few studies of comprehensive treatment programmes.

#### Aims

To examine the effect of a comprehensive cognitive-behavioural treatment (CCBT) programme compared with placebo-controlled mirtazapine medication in patients with chronic fatigue, and to study the effect of combined medication and CCBT.

#### Method

A three-armed randomised clinical trial of mirtazapine, placebo and a CCBT programme was conducted to investigate treatment effect in a patient group (n=72) with chronic fatigue referred to a specialist clinic. The CCBT programme was compared with mirtazapine or placebo therapy for 12 weeks, followed by 12 weeks treatment with a mixed crossover-combination design. Assessments were done at 12 weeks and 24 weeks.

#### Results

By 12 weeks the treatment effect was significantly better in the group initially receiving CCBT, as assessed with the Fatigue Scale (P=0.014) and the Clinical Global Impression Scale (P=0.001). By 24 weeks the treatment group initially receiving CCBT for 12 weeks followed by mirtazapine for 12 weeks showed significant improvement compared with the other treatment groups on the Fatigue Scale (P=0.001) and the Clinical Global Impression Scale (P=0.002). Secondary outcome measures showed overall improvement with no significant difference between treatment groups.

#### Conclusions

Multimodal interventions may have positive treatment effects in chronic fatigue syndrome. Sequence of interventions seem to be of importance.

#### Declaration of interest

The trial received an unrestricted grant from Organon AS, who provided the placebo-controlled medication.