

# Effect of Yokukansan, a Traditional Herbal Prescription, on Sleep Disturbances in Patients with Alzheimer's Disease

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## Abstract

**Objective:** Evidence of the effects of Yokukansan (YKS), a traditional herbal medicine, on behavioral and psychological symptoms of dementia (BPSD) has accumulated. As well as BPSD, patients with Alzheimer's disease (AD) can be prevalent in the elderly. PLMs are generally considered to produce sleep fragmentation by provoking arousals. This study aimed to examine whether YKS alters polysomnography variables in patients with AD.

**Methods:** Seven patients (3 men and 4 women) with probable AD according to the standard criteria were investigated. Participants were treated with YKS for 4 weeks. The Neuropsychiatric Inventory for the assessment of BPSD, the Mini-Mental State Examination (MMSE) for cognitive function, polysomnography for evaluation of sleep structure and Pittsburgh Sleep Quality Index (PSQI) for subjective sleep quality, and Epworth Sleepiness Scale (ESS) were carried out at baseline and at the end of the treatment. The local institutional review boards approved this study. All patients gave written consent according to institutional guidelines and the tenets of the Declaration of Helsinki.

**Results:** Treatment with YKS resulted in a decreased NPI score, a prolonged total sleep time, a shortened sleep latency, and improved subjective evaluations with PSQI and ESS.

**Conclusions:** YKS was effective for BPSD and sleep disturbances in patients with AD. YKS did not induce daytime somnolence, extrapyramidal signs, or an increased apnea-hypopnea index.

**Keywords:** Alzheimer's disease; Behavioral and psychological symptoms of dementia (BPSD); Fragmentation of sleep; Herbal medicine; Polysomnography; Sleep disturbance; Yokukansan

**Abbreviations:** BPSD: Behavioral and psychological symptoms of dementia; 5-HT<sub>2A</sub>: 5-hydroxytryptamine 2A receptor; GABA: gamma-aminobutyric acid; MMSE: Mini-Mental State Examination; NPI: Neuropsychiatric Inventory; PLMS: Periodic Limb Movements during Sleep; PSG: Polysomnography; PSQI: Pittsburgh Sleep Quality Index; YKS: Yokukansan

## Introduction

It is well known that sleep disturbances are common in patients with Alzheimer's disease (AD) and behavioral and psychological symptoms of dementia (BPSD). Sleep disturbances in AD are characterized by fragmented sleep, reduced total sleep time, and increased awakenings [1]. Sleep disturbances in AD are associated with cognitive decline and increased risk of mortality [2].

Yokukansan (YKS), a traditional Japanese herbal medicine, has been shown to improve sleep quality and reduce BPSD in AD patients [3]. YKS is composed of several herbs, including GABA and 5-HT<sub>2A</sub> receptor antagonists. The mechanism of action of YKS is thought to be related to its effects on the GABAergic and serotonergic systems [4].

The present study aimed to examine the effects of YKS on sleep disturbances in AD patients. We hypothesized that YKS would improve sleep quality and reduce BPSD in AD patients.

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**Received** January 27, 2016; **Accepted** February 29, 2016; **Published** March 07, 2016

**Citation:** Shinno H, Ishikawa I, Ando N





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