

Review

Concerns about the use of buspirone in Alzheimer patients *

Ian Williams Goddard

Rockville, MD, USA

Abstract. The antianxiety drug buspirone is favored for anxious patients with Alzheimer's disease (AD) because it is less sedating than the benzodiazepine tranquilizers, which may worsen cognitive impairment. But how safe is buspirone for AD patients? A review of medical research finds several prominent similarities between AD pathology and buspirone pharmacology, raising concerns that buspirone could significantly augment cognitive decline in AD.

1. Background

Alzheimer's disease (AD) is the most common form of dementia, afflicting approximately four million people in the US alone [1]. AD occurs primarily in the elderly, manifesting itself initially as mild cognitive impairment (MCI) and progressing eventually to profound dementia.

The purpose of this report is to address possible dangers regarding the use of the drug buspirone by AD patients.

2. Review

Buspirone, marketed as an "antianxiety" drug, is pharmacologically distinct from the benzodiazepines, the most widely prescribed antianxiety and tranquilizing drugs. Buspirone is often recommended for AD patients because it is less sedating than the benzodiazepines [6]. Buspirone has also been shown to cause less cognitive impairment in healthy subjects than the benzodiazepines [29]. Nevertheless, buspirone suppresses neurological function and interferes with communication between brain cells, primarily in a region of the brain known as the hippocampus – a fact that signals possible danger for AD patients.

The hippocampus is central to memory functions [14] and is a primary site of AD-associated pathology [11,26]. AD-induced hippocampal degradation is manifested as a reduction of neuronal activity in the hippocampus, which may be the initial onset pathology of AD [22,27].

In light of the above, it is noteworthy that buspirone has been shown to systematically reduce neuronal activity in the hippocampus [8,15,26,28]. Buspirone-induced hippocampal suppression has also been shown to increase during chronic exposure, which may contribute to the delayed onset of its therapeutic effect [19]. This is significant, for if hippocampal suppression is involved in the therapeutic mechanism

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of buspirone, then, if doctors determine that the drug is working, it is probable that hippocampal suppression would be occurring. In short, consistent with Peter Breggin's first principle of brain-disabling treatments [4], the evidence suggests that brain impairment and "therapeutic effect" may be the same thing.

It is worth observing that evidence suggests that marijuana impairs memory by suppressing neuronal activity in the hippocampus [7]. Establishing a consistent correlation between hippocampal suppression and memory impairment, buspirone has been shown to impair memory in both animals and humans [2, 9,12,13,21,24,29,30,32].

Sellers et al. [24] found that a single dose of buspirone equal to one third the maximum recommended daily intake caused significant memory impairment in healthy subjects. Holland et al. [9] found that a therapeutic dose of buspirone adversely affected a range of cognitive tests including logical reasoning in healthy subjects. It should be noted that the elderly and ill are more vulnerable than the young and healthy to the cognitive-impairing effects of drugs [18].

It has also been shown: (a) that buspirone reduces serotonin in the hippocampus [25], and AD is associated with reduced serotonin in the hippocampus [3]; (b) that buspirone reduces the number of active 5-HT_{1A} serotonin receptors in the hippocampus [25], and AD is associated with a reduced number of active 5-HT_{1A} receptors in the hippocampus [33]; (c) that buspirone increases the hormone cortisol [16], and increases of cortisol correspond with increased cognitive impairment in AD [5,17,31].

3. Conclusions

To summarize, research indicates that both Alzheimer's disease and buspirone appear to share at least five common effects:

- (1) impairment of memory,
- (2) reduction of neuronal activity in the hippocampus,
- (3) reduction of hippocampal serotonin,
- (4) reduction of active 5-HT_{1A} receptors in the hippocampus,
- (5) increase of the hormone cortisol.

The evidence therefore suggests that the use of buspirone by AD patients could promote those deleterious effects of AD. More specifically, since at least points 1 through 4 above are linked to the "therapeutic" effect of buspirone, the effectiveness of buspirone treatment appears to rest on the occurrence of AD-like effects. Because there appears to be little or no research on the cognitive impact of buspirone in AD patients, extrapolation based upon known effects of buspirone may be the best method of risk assessment at this time.

The danger remains that in AD patients, drug-induced cognitive impairments will go unnoticed due to their similarity to AD pathology. This emphasizes the wisdom of minimizing or ideally avoiding the use in AD patients of any drugs that are even mildly deleterious to cognitive function.

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