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Commentary Open Access

Commentary: Over-diagnosis and Under-Diagnosis of Alzheimer's Disease

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Abstract

Alzheimer's Disease (AD) is diagnosed by criteria of DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) or NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association) Work Group. Clinically, this disorder is diagnosed by forgetfulness and disturbances of daily livings. However, we feel there existence at substantial level of over-diagnosis and under-diagnosis of AD. Therefore in this article, we discuss the reasons why over-diagnosis and under-diagnosis of AD is occurred. We consider that over-diagnosis of AD is occurred when we misdiagnose the depression or bipolarity. On the contrary, we consider that under-diagnosis of AD is occurred when we overlook apathy. We also feel that the most problem is that many physicians diagnose AD based only on the cognitive functions and diagnostic imaging in clinical setting but not on apathy symptoms of everyday life. In order to prevent these states, we should hear behaviours in everyday life and life history of the patient because apathy and depression are not always seen in clinical settings. Therefore, we consider that we should not misdiagnose depression and not overlook apathy founded out in everyday life at patients or persons with old age.

Abbreviations: ACh: acetylcholine; AD: Alzheimer's disease; BPSD: behavioral and psychological symptoms of dementia; BT: bipolarity; ChAT: choline acetyltransferase; ChEI: cholinesterase inhibitor; MCI: mild cognitive impairment

Keywords: Alzheimer's disease; Over diagnosis; Under diagnosis

Commentary

Alzheimer's disease (AD) is diagnosed by DSM-5 [1] or NINCDS-ADRDA Work Group [2]. Clinically, this disorder is diagnosed by forgetfulness and disturbances of daily livings. However, we feel there existence at substantial level of over-diagnosis and under-diagnosis of AD. Therefore in this article, we discuss the reasons why over-diagnosis and under diagnosis of AD is occurred.

We consider that over diagnosis of AD is occurred when we misdiagnose the depression or bipolarity [3] (BT). Depression is tended to develop AD [4] and when depression occurs, cognitive dysfunctions also occur, which is same as those of AD (pseudo-dementia) [5, 6]. On the elderly persons, not only BT but also aging process cause pseudo-demented state. Moreover, this state is also similar with the symptoms of AD. In this state, when we prescribe cholinesterase inhibitors (ChEI), agitation and aggressiveness are occurred sometimes. We emphasize that we should find out BT.

We consider that under diagnosis of AD is occurred when we overlook the apathy. We also feel that the major problem is that many physicians diagnose AD based only on the cognitive functions and diagnostic imaging in clinical setting but not on apathy symptoms founded out in everyday life. As mentioned before, AD pathology causes the degeneration of cholinergic neurons. However, because the compensatory mechanism works, the activity of choline acetyltransferase (ChAT, an enzyme that produces acetylcholine (ACh)) is not down regulated in the mild to moderate stages of AD [7,8]. According to this compensatory mechanism, at mild stage of AD, ChAT activity in AD patients could have been high, which could account for the fact that the ACh level was relatively normal and in ordinal situations, cognitive functions in AD patients were relatively intact. This compensatory reaction to the onset of AD may be attributable to hyperactivity of presynaptic cholinergic neurons. If this compensatory mechanism works, the cholinergic system is intact, rather than deteriorated. However, if this compensatory mechanism continues, continuation of hyperactivity cholinergic neurons causes early degenerations of these neurons because of fatigue. If we can prescribe ChEI, the compensatory mechanism can be mild and prevention of early degeneration of cholinergic neuron is possible. Therefore, we should not overlook this state when we diagnose AD. We speculate that there might be two situations in which ACh might be down regulated or overburdened [9]. We show this in (Figure 1). In mild cognitive impairment (MCI) stage (Figure 1, middle) there are two occasions for diagnosis of AD, those are not seen in the normal stage (Figure 1, left). One occurs when patients with AD at the MCI stage relax, at which time the ACh level is lower than normal. In this situation, these patients show apathy (e.g., when they watch television, they fall asleep). The other situation is when they are more stressed than usual. In this situation, their cholinergic system cannot be up regulated any further because ChAT is already activated and does not permit further upregulation and the patient shows depressive symptoms. Moreover, there is the possibility that the patient faces delusion, hallucination and aggression [10,11]. When ChEIs are prescribed, ACh upregulation is possible, even if another stressful factor is present, to compensate for this insert and ameliorate stress (Figure 1, right). We reported that behavioral and psychological symptoms of dementia (BPSD) is caused by BT or AD pathology [10,11]. In fact, after the patient show these BPSD, the progression of AD is accelerated. Moreover, when the patient complains the subjective memory complains, we should start the treatment for AD [12].

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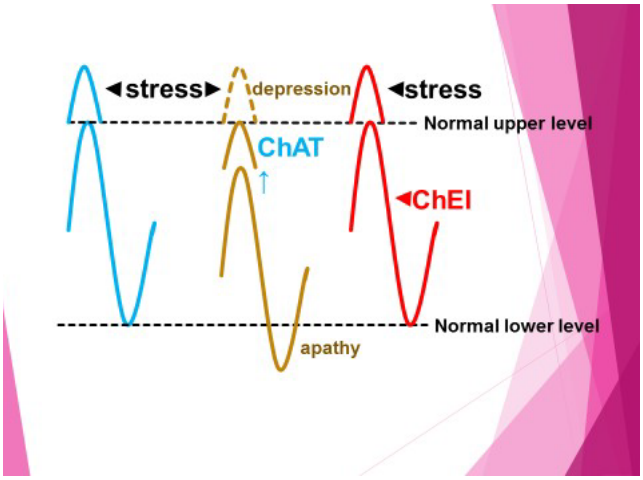

Figure 1: In mild cognitive impairment (MCI) stage (middle) there are two occasions for diagnosis of Alzheimer's disease (AD) those are not seen in the normal stage (left). One occurs when patients with AD at the MCI stage relax, at which time the acetylcholine (ACh) level is lower than normal. In this situation, these patients show apathy (e.g., when they watch television, they fall asleep). The other situation is when they are more stressed than usual. In this situation, their cholinergic system cannot be up regulated any further because cholin acetyltransferase (ChAT in the figure) is already activated and does not permit further upregulation and the patient shows depressive symptoms. Moreover, there is the possibility that the patient delusion, hallucination and aggression. When cholinesterase inhibitors (ChEI in the figure) are prescribed, ACh upregulation is possible, even if another stressful factor is present, to compensate for this insert and ameliorate stress (right). This article is reproduced from Hori et al. [9].

In order to prevent over-diagnosis and under diagnosis of AD, we should hear their behaviors in everyday life and life history of the patient. Apathy and depression are not always seen in clinical settings. These symptoms are shown in their everyday lives.

Therefore, we consider it is important that we should not misdiagnose depression and not overlook apathy founded out in every life of patients or persons with old age. Alternatively these procedures are painful. Therefore, it is difficult for early diagnosis of elderly subjects with mild cognitive impairment [13]. However, these processes are interesting as for psychiatrist because we can see the lives of patients who live longer lives.

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