# Anosmia in dementia is associated with Lewy bodies rather than Alzheimer's pathology

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**Abstract**

***Objectives*—To assess olfactory function of patients with dementia. Odour detection ability is impaired in clinical Parkinson's disease. Evidence of impaired detection in patients with clinically diagnosed Alzheimer's disease is inconsistent. No studies of olfaction have been neuropathologically validated.**

***Methods*—The olfactory function of 92 patients with dementia and 94 controls was assessed using a simple bedside test as part of the Oxford Project To Investigate Memory and Ageing (OPTIMA). Neuropathological assessment was made of cortical Lewy bodies and substantia nigra (SN) cell counts and of Alzheimer's disease in all 92 patients, 22 of whom had SN Lewy bodies and 43 of whom had only Alzheimer's disease.**

***Results*—Patients with Lewy bodies were more likely to be anosmic than those with Alzheimer's disease or controls. Patients with Alzheimer's disease were not more likely to be anosmic than controls. Nor was anosmia associated with degree of neurofibrillary tangles, as assessed by Braak stage. Among subjects with Lewy bodies, overall cortical Lewy body scores and Lewy body density in the cingulate were higher in those who were anosmic. Consensus clinical criteria for dementia with Lewy bodies had a sensitivity of 64% and specificity of 89%. In the absence of definite Alzheimer's disease, the criteria had sensitivity of 100%. In patients with definite Alzheimer's disease, anosmia was slightly more sensitive (55%) than the consensus criteria (33%). However, the addition of anosmia to the consensus criteria did not improve their overall performance.**

***Conclusion*—Dementia with Lewy bodies is associated with impaired odour detection. Misdiagnosis may have accounted for some previous reports of impaired odour detection in Alzheimer's disease. Simple but more sensitive tests of anosmia are required if they are to be clinically useful in identifying patients with dementia with Lewy bodies.**

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There are three main domains of olfactory function: the ability to detect an odour, the ability to recognise it, and the ability to identify it. Anosmia represents the most severe impairment of detection. There is good evidence that impaired odour detection in Parkinson's disease is not simply due to poor cognitive function.[1 2] The picture is less clear in Alzheimer's disease. Impaired recognition and identification of odours is influenced by cognitive function in Alzheimer's disease[3] and there is contradictory evidence on the question of impaired detection,[4–9] which may depend on which odour is tested.[10]

There have not been any studies of olfactory function in Parkinson's disease or Alzheimer's disease in which the diagnosis was neuropathologically validated. This could be important as 24% of patients with a clinical diagnosis of idiopathic Parkinson's disease do not have Lewy body pathology[11] and clinical diagnostic criteria for Alzheimer's disease commonly fail to identify patients with Lewy body pathology.[12 13]

The aim of this study was therefore to investigate the association of anosmia with the presence of Lewy bodies and Alzheimer-type pathology in patients with dementia, taking into account the effects of impaired cognitive function.

## Method

The Oxford Project to Investigate Memory and Ageing (OPTIMA) is a longitudinal study of patients with dementia with a high necropsy rate (94%). Patients (n=92) had neuropathologically confirmed neurodegenerative dementia and full clinical datasets, including a score of at least 2 on the dementia scale of Blessed (DSB),[14] and a mini mental state examination (MMSE)[15] score below 24 at some point before death. Controls were over 65 and never fulfilled either the DSB or MMSE criterion.

All patients were asked whether they could smell anything from a sniff botle containing lavender water and were regarded as anosmic if they could not. The lavender water was a preparation of 1.7% lavender oil in denatured ethanol from a chain of large national pharmacies (Boots PLC) and was replaced every 3 to 6 months. The test was repeated a year later in 58 patients, giving an index of test-retest reliability. The performance of this test in controls was compared with the rate of anosmia that would be expected using the scratch and sniff University of Pennsylvania smell identification test (UPSIT).[16]

A clinical diagnosis of probable dementia with Lewy bodies was based on the presence of any two of the following at study entry[17]: visual hallucinations for at least 4 months, persistent brief fluctuations in cognitive or functional

ability lasting minutes or hours (item 272 of the Cambridge mental disorders of the elderly examination CAMDEX[18]), and at least one feature of parkinsonism.

Alzheimer's disease pathology was assessed according to the CERAD[19] and modified Braak protocols.[20] A 10 point cortical Lewy body score was derived from assessments of five sections (anterior cingulate gyrus, parahippocampal gyrus, insular, middle frontal, middle temporal, and visual association cortex stained for ubiquitin) using the consensus guidelines[17] with two variations. Firstly, except for the cingulate, a 0.5 cm cortical strip rather than a strip from the sulcus to the crest of the gyrus was examined in all areas because sulcal depth is highly variable. Secondly, Lewy body pathology was not assessed in the parietal cortex and counts from the visual association cortex were substituted in determining the score. Olfactory bulbs were not available. Cortical Lewy bodies and pigmented nucleated cells in the whole SN were counted blind to clinical data and data from every other section from the same patient. Patients were defined as having neuropathological dementia with Lewy bodies if any Lewy bodies were identified in both the SN and the cingulate gyrus.

Analyses of the associations of Alzheimer's disease and Lewy body pathology with anosmia were restricted to patients with either probable or definite Alzheimer's disease or with Lewy bodies (n=65). Analyses of the diagnostic utility of anosmia drew on data from the whole sample of 92.

## Results

Most patients, 58% of whom were women, were referred by general practitioners (35%) or psychiatrists (40%). The mean (SD) age, MMSE, and CAMCOG[18] at study entry were 75.6 (8.0) years, 15.1 (7.6), and 51.8 (26.6) respectively. The mean duration after study entry until death was 2.6 (1.4) years. Controls were well matched to the sample of patients with dementia on sex (59% women) and age (mean 75.3 (5.9)). Lewy bodies were detected in the substantia nigra of 22 (24%) patients with dementia, 17 (77%) of whom also had Lewy bodies in the cingulate, 16 (73%) of whom had probable or definite Alzheimer's disease, and all except one (5%) of whom had at least some neurofibrillary tangles on Braak staging. Of the remaining 70, 43 had probable or definite Alzheimer's disease only, two had possible Alzheimer's disease only, eight had Alzheimer's disease plus other conditions (five vascular), and 17 had no Alzheimer's disease (seven vascular, three frontal lobe dementia, one normal pressure hydrocephalus, one previously unsuspected Huntington's disease, one progressive supranuclear palsy, four cause unknown).

Patients with Lewy bodies were more likely to be anosmic than controls (41% *v* 6%; p<0.0001) or those with Alzheimer's disease (16%; p=0.029, table 1). Those with Alzheimer's disease were not more likely to be anosmic than controls although there was a trend in this direction (p=0.13). The possibilities that the association of anosmia with Lewy bodies in dementia was due to sex, impaired cognitive function, or age were examined and excluded. Although men were more likely to be anosmic than women (10/27 *v* 6/32; $\chi^2$ =3.8; p=0.050), they were not more likely to have Lewy body pathology (11/27 *v* 11/38;$\chi^2$ =0.98; p=0.32). The CAMCOG score was no worse in those who were anosmic (n=49) than in those who were not (n=16) (50.6(25.5) *v* 42.5(27.2); *t*=−1.1, df=63, p=0.29). There was no difference in the age of those who were or were not anosmic (76.8 (9.8) *v* 75.4 (7.3)). Those with Lewy body pathology did not have better cognitive function (CAMCOG=47.3 (23.8)) than those with Alzheimer's disease only (49.2 (27.2); df=63, *t*=0.27, p=0.8). Cohen's κ for the test-retest reliability of anosmia after 1 year was 0.52. Controls were less likely to fail to detect lavender (n=6) than would be expected to be anosmic on the UPSIT (n=15).

*Table 1 Number of patients with anosmia*

| | *Anosmia* | |
|---|---|---|
| | *Absent* | *Present* |
| Controls | 88 | 6 |
| Pure AD | 36 | 7 |
| LBs | 13 | 9 |

AD=Alzheimer's disease; LBs=Lewy bodies.
Anosmia statistics: overall $\chi^2$=18.12, df=2, p=0.0001; LB *v* control $\chi^2$=15.9, df=1, p<0.0001; AD *v* control $\chi^2$=2.31, df=1, p=0.13; LB *v* AD $\chi^2$=4.76, df=1, p=0.029 (Yates correction applied when any cell with expected value<5).

The possibility that coexisting Alzheimer's disease pathology contributed to the association of Lewy body pathology with impaired olfaction was examined further and excluded. In the sample of 65 with pure Alzheimer's disease or Lewy bodies the severity of neurofibrillary pathology was not different in those with and without anosmia (Braak stage: 4.3 (1.2) *v* 4.5(1.4); Mann Whitney *U*=288, *z*=−1.18; p=0.24). Separate analyses on those with Lewy bodies (n=20, two patients with missing Braak data), and those with Alzheimer's disease only (n=43) also failed to show any relation between severity of neuropathological Alzheimer's disease and anosmia (patients with Lewy bodies: Braak stage=3.5 (1.0) *v* 3.7(1.9); Mann Whitney *U*=41, *z*=−0.51, p=0.62. Alzheimer's disease only: Braak stage=5.2 (0.42) *v* 4.8(1.1); Mann Whitney *U*=118, *z*=−0.27, p=0.81). Finally, the possibility that Alzheimer's disease and Lewy body pathology acted synergistically to produce anosmia was examined and excluded. Those with both Lewy body and Alzheimer's disease were no more likely to be anosmic (seven of 16 patients) than those with Lewy body but without Alzheimer's disease (two of six patients) (Fisher's exact p=1.0).

The relative contributions of cortical Lewy body pathology and SN cell loss to anosmia were examined in the sample of patients with Alzheimer's disease or dementia with Lewy bodies (n=65). There was a strong association between anosmia and a higher cortical Lewy

body score (3.3 (2.7) *v* 1.3 (1.8); Mann Whitney *U*=188, z=−3.1, p=0.002). The SN cell counts were also lower in those with anosmia (318 (178) v 471(218); df 58, *t*=−2.4, p=0.02). Confining the sample to the 22 patients with Lewy bodies in the SN, the mean cortical Lewy body score was greater in the nine patients with anosmia (4.8 (2.4) *v* 2.5 (2.5); *t*=2.1, df=20, p=0.05), but there was no significant difference in the SN cell count (242 (119) *v* 308 (126); *t*=−1.2, df=19, p=0.24).

Logistic regression analyses were performed, in which the dependent variable was anosmia. The following independent variables were entered in a forward conditional analysis: mean SN cell count, cortical Lewy body score, Braak Alzheimer's disease stage, sex, CAMCOG, and age at study entry. In the final model, cortical Lewy body score (B=−0.48, SE=0. 18, Wald=7.09, df=1, p=0.008) and sex (B=1.93, SE=0.83, Wald=5.4, df = 1, p=0.02) contributed independently to the presence of anosmia, but the other variables did not. The results were unaltered in simultaneous entry and backward stepwise analyses and by omission of CAMCOG score from the variable list.

An exploratory analysis of cortical Lewy body density in individual brain areas showed that anosmic patients had significantly greater density of cortical Lewy bodies in the cingulate gyrus than those without (mean density Lewy body/mm$^2$= 0.64 (0.59) *v* 0.27 (0.54); Mann Whitney *U*=25, *z*=−2.25, p=0.025). This was not apparent in the other five cortical areas examined.

The consensus criteria for probable dementia with Lewy bodies[17] performed very well in patients without CERAD definite Alzheimer's disease, identifying all patients with Lewy body in the SN and cingulate (sensitivity=100%, PPV=73%). The criteria were specific but lacked sensitivity in patients with definite Alzheimer's disease (table 2). Overall, the positive predictive value of anosmia was only 43%. In patients with CERAD definite Alzheimer's disease, anosmia was slightly more sensitive (55%) than the consensus criteria for dementia with Lewy bodies (33%). A new criterion for probable dementia with Lewy bodies that included anosmia and demanded two of four symptoms (parkinsonism, visual hallucinations, fluctuation, and anosmia) identified two more true positive patients than the existing criteria, but also yielded two more false positives.

*Table 2 Performance of consensus clinical diagnostic criteria for DLB and of anosmia*

| | *Consensus DLB criteria** | *Anosmia* |
|---|---|---|
| All cases (n=92): | | |
| Sensitivity | 64 | 53 |
| Specificity | 89 | 84 |
| PPV | 58 | 43 |
| Definite AD(n=54)† | | |
| Sensitivity | 33 | 55 |
| Specificity | 88 | 82 |
| PPV | 38 | 38 |
| Not definite AD (n=38) | | |
| Sensitivity | 100 | 50 |
| Specificity | 90 | 87 |
| PPV | 73 | 50 |

AD=Alzheimer's disease; DLB=dementia with Lewy bodies; PPV=positive predictive value (%); neuropathological criterion for DLB=LBs present in both SN and cingulate gyrus. *At least two of visual hallucinations for at least 4 months, persistent brief fluctuations (item 272 of CAMDEX), and at least one feature of parkinsonism.
†CERAD criteria for definite AD.

## Discussion

This is the first clinicopathological series to correlate olfactory function in life with necropsy findings. Our results confirm the presumed association of impaired olfactory function with Lewy body pathology, and show that this association extends to patients with dementia as well as those with clinical Parkinson's disease. One explanation for the surprising discrepancy between our data and those clinical studies which have found impaired odour detection in Alzheimer's disease may lie in the failure of clinical criteria for Alzheimer's disease to exclude patients with Lewy body pathology.

Why is dementia with Lewy bodies, but not Alzheimer's disease, associated with anosmia? There are no olfactory brain areas that are heavily affected by Lewy bodies in dementia with Lewy bodies, but remain unaffected in patients with pure Alzheimer's disease. The possibility of an additive effect on olfactory function of Alzheimer's disease and Lewy body pathology is attractive as, in this series, all patients with Lewy bodies except one also had at least some Alzheimer's disease pathology. Different neurons in the anterior olfactory nucleus or olfactory cortices might be affected by Lewy bodies and tangles,[21] or, in the amygdala, both abnormalities may be present in the same cells.[22] However, this hypothesis is not supported by either simple $\chi^2$ or regression analyses of our data on cortical pathology. Although Lewy body involvement and cell loss in the anterior olfactory nucleus is extensive in Parkinson's disease, with almost complete group separation from controls,[23] cell loss and tangle formation are also more severe in the olfactory bulb of those with Alzheimer's disease than controls.[24 21] Unfortunately the loss of olfactory bulbs during processing and storage made it impossible to examine the effect of additive pathology in peripheral structures.

Our failure to find an association of anosmia with Braak Alzheimer's disease stage could be explained if a ceiling in the effect on olfactory function of Alzheimer's disease (anosmia) is reached at very early Braak stages. However, this possibility would contradict data from clinical studies which show that olfactory dysfunction is correlated with degree of dementia in those with established Alzheimer's disease.[10 25] Furthermore, without doing olfactory bulb biopsies, or large clinicopathological studies of controls, this explanation is untestable.

Odour detection may be dependent on dopaminergic neurons, which are selectively affected by Lewy bodies.[26] The anterior cingulate, a predilection site of Lewy bodies, is rich in dopaminergic innervation, which may explain our finding of increased cingulate Lewy body density in patients with anosmia. The

cingulate and frontal regions are activated by odours in normal volunteers, as well as regions previously recognised as olfactory cortex (entorhinal and orbitofrontal).[27] In patients with hyposmia, activation is reduced in the cingulate, orbitofrontal, medial temporal, and posterior temporal regions, but is restored when olfactory function is improved.[28]

A strength of the study was the standardised assessment of fluctuation, which, although it is a core feature of dementia with Lewy bodies in the consensus clinical criteria,[17] is difficult to define. We found that short term fluctuations lasting "minutes or hours" segregated with other elements of the clinical syndrome of dementia with Lewy bodies and were associated with Lewy body pathology whereas longer fluctuations of "hours or days" were not. The within patient blinding of pathological assessment was also a strength. It reduced the possibility of confounds due to confusion of ubiquitinated globose tangles and cortical Lewy bodies. Although α-synuclein immunohistochemistry may have been more sensitive, it was not available at the time of this work, and there are emerging doubts about its specificity for Lewy bodies.[29 30] The only report comparing ubiquitin and α-synuclein in the cortex found similar numbers of Lewy bodies staining with each.[31]

The main limitation of the present study lies in the method of olfactory testing. As there were no dummy bottles, suggestibility and response bias could not be ruled out, but the cognitive function of the Alzheimer's disease and dementia with Lewy bodies groups was not different and there is no obvious reason why those with Alzheimer's disease should be more likely to say that they could detect an odour than those with dementia with Lewy bodies. Conventional tests of detection threshold use sequential presentation of differing concentrations of odorants but these longer tests, although more reliable,[32] would not be feasible for patients with dementia. The test-retest reliability over a year ($\kappa$=0.52) was modest but is likely to be confounded by patients who genuinely developed anosmia over that period, and was better than the 2 week reliability of single ascending butanol detection threshold tests in normal subjects.[32] Fewer controls were anosmic on this test than expected, suggesting that the olfactory stimulus might have been of a higher concentration than occurs in UPSIT and raising the possibility that some patients reported detection of the odour because of a trigeminal effect. Such an effect would have worked against detection of an association of anosmia with Lewy bodies.

The main problem with the existing clinical diagnostic criteria for dementia with Lewy bodies is poor sensitivity due to the masking of symptoms by concomitant Alzheimer's disease (table 2). The crude test we used did not improve the predictive value of the criteria. Odours such as pizza and wintergreen may be better at discriminating patients with Parkinson's disease from controls,[2] although this awaits confirmation. It is not known whether these would be better discriminators between Alzheimer's disease and dementia with Lewy bodies than the test that we used as reports of reduced odour sensitivity in Alzheimer's disease depend on the odour being tested.[10] The finding that patients with dementia with Lewy bodies were less likely than those with Alzheimer's disease to be able to detect lavendar on a classic bedside test holds out the possibility that a simple test may yet be developed which has the right sensitivity profile to be a useful addition to existing diagnostic criteria.

Smells are probably less well semantically encoded in humans than other stimuli, making olfactory recognition and identification relatively more vulnerable to early Alzheimer's disease than detection.[8 33] This also explains why tests of odour identification may be markers for subsequent cognitive decline.[34 35]

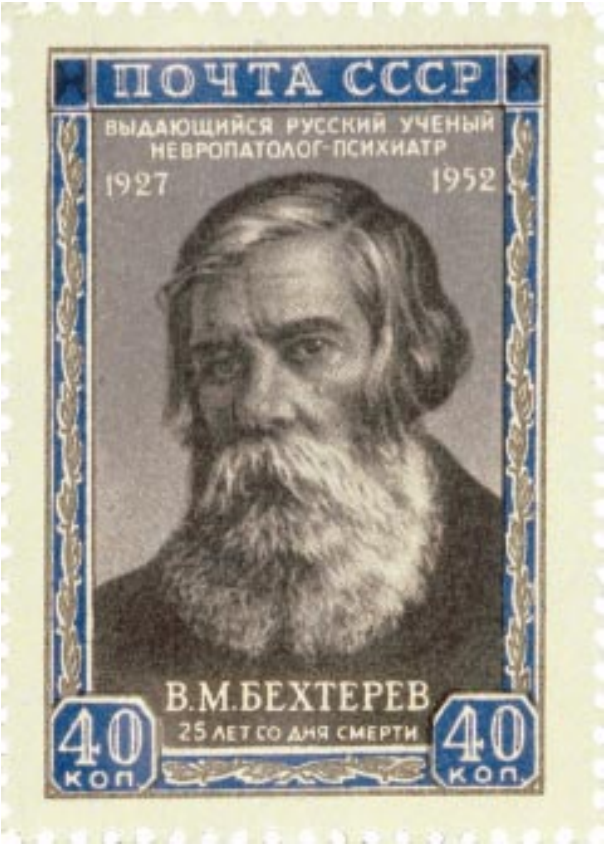
Nevertheless, given that detection is a prerequisite for identification, our results suggest that neuropathological validation is necessary before any impairments in olfactory function can be confidently attributed to Alzheimer's disease rather than dementia with Lewy bodies.


1 Doty RL, Riklan M, Deems DA, *et al*. The olfactory and cognitive deficits of Parkinson's disease: evidence for independence. *Ann Neurol* 1989;**25**:166–71.
2 Hawkes CH, Shephard BC, Daniel SE. Olfactory dysfunction in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1997;**62**:436–46.
3 Serby M, Larson P, Kalkstein D. The nature and course of olfactory deficits in Alzheimer's disease. *Am J Psychiatry* 1991;**148**:357–60.
4 Doty RL, Reyes PF, Gregor T. Presence of both odor identification and detection deficits in Alzheimer's disease. *Brain Res Bull* 1987;**18**:597–600.
5 Nordin S, Monsch AU, Murphy C. Unawareness of smell loss in normal aging and Alzheimer's disease: discrepancy between self-reported and diagnosed smell sensitivity. *J Gerontol B Psychol Sci Soc Sci* 1995;**50**:187–92.
6 Koss E, Weiffenbach JM, Haxby JV, *et al*. Olfactory detection and identification performance are dissociated in early Alzheimer's disease. *Neurology* 1988;**38**:1228–32.
7 Rezek DL. Olfactory deficits as a neurologic sign in dementia of the Alzheimer type. *Arch Neurol* 1987;**44**:1030–2.
8 Larsson M, Semb H, Winblad B, *et al*. Odor identification in normal aging and early Alzheimer's disease: effects of retrieval support. *Neuropsychology* 1999;**13**:47–53.
9 Mesholam RI, Moberg PJ, Mahr RN, *et al*. Olfaction in neurodegenerative disease: a meta-analysis of olfactory functioning in Alzheimer's and Parkinson's diseases. *Arch Neurol* 1998;**55**:84–90.
10 Nordin S, Almkvist O, Berglund B, *et al*. Olfactory dysfunction for pyridine and dementia progression in Alzheimer disease. *Arch Neurol* 1997;**54**:993–8.
11 Hughes AJ, Daniel SE, Kilford L, *et al*. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry* 1992;**55**:181–4.
12 Joachim CL, Morris JH, Selkoe DJ. Clinically diagnosed Alzheimer's disease: autopsy results in 150 cases. *Ann Neurol* 1988;**24**:50–6.
13 Gibb WR, Mann DM, Mountjoy CQ, *et al*. A pathological study of the association between Lewy body disease and Alzheimer's disease. *Adv Neurol* 1990;**53**:55–9.
14 Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and senile changes in the cerebral grey matter of elderly subjects. *Br J Pschol* 1968;**225**:797–811.
15 Folstein MF, Folstein SE, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;**12**:189–98.
16 Doty RL, Shaman P, Kimmelman CP, *et al*. University of Pennsylvania smell identification test: a rapid quantitative olfactory function test for the clinic. *Laryngoscope* 1984;**94**:176–8.
17 McKeith IG, Galasko D, Kosaka K, *et al*. Consensus guidelines for the clinical and pathological diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. *Neurology* 1996;**47**:1113–24.
18 Roth M, Tym E, Mountjoy CQ, *et al*. CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *Br J Psychiatry* 1986;**149**:698–709.
19 Mirra SS, Heyman A, McKeel D, *et al*. The consortium to establish a registry for Alzheimer's disease (CERAD). II. Standardisation of neuropathological assessment of Alzheimer's disease. *Neurology* 1991;**41**:479–86.

20 Nagy Z, Yilmazer HD, Braak H, *et al*. Assessment of the pathological stages of Alzheimer's disease in thin paraffin sections: a comparative study. *Dement Geriatr Cogn Disord* 1998;**9**:140–4.
21 Kovács T, Cairns NJ, Lantos PL. β-Amyloid deposition and neurofibrillary tangle formation in the olfactory bulb in ageing and Alzheimer's disease. *Neuropathol Appl Neurobiol* 1999;**25**:481–91.
22 Schmidt ML, Martin JA, Lee VM, *et al*. Convergence of Lewy bodies and neurofibrillary tangles in amygdala neurons of Alzheimer's disease and Lewy body disorders. *Acta Neuropathol Berl* 1996;**91**:475–81.
23 Pearce RK, Hawkes CH, Daniel SE. The anterior olfactory nucleus in Parkinson's disease. *Mov Disord* 1995;**10**:283–7.
24 Esiri MM, Wilcock GK. The olfactory bulbs in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 1984;**47**:56–60.
25 Murphy C, Gilmore MM, Seery CS, *et al*. Olfactory thresholds are associated with degree of dementia in Alzheimer's disease. *Neurobiol Aging* 1990;**11**:465–9.
26 Kuljis RO, Martin-Vasallo P, Peress NS. Lewy bodies in tyrosine hydroxylase-synthesizing neurons of the human cerebral cortex. *Neurosci Lett* 1989;**106**:49–54.
27 Yousem DM, Maldjian JA, Hummel T, *et al*. The effect of age on odor-stimulated functional MR imaging. *AJNR Am J Neuroradiol* 1999;**20**:600–8.
28 Levy LM, Henkin RI, Hutter A, *et al*. Mapping brain activation to odorants in patients with smell loss by functional MRI. *J Comput Assist Tomogr* 1998;**22**:96–103.
29 Takeda A, Hashimoto M, Mallory M, *et al*. C-terminal α-synuclein immunoreactivity in structures other than Lewy bodies in neurodegenerative disorders. *Acta Neuropathol* 2000;**99**:296–304.
30 Mukaetova-Ladinska EB, Hurt J, Jakes R, *et al*. α-Synuclein inclusions in Alzheimer and Lewy body diseases. *J Neuropathol Exp Neurol* 2000;**59**:408–17.
31 Spillantini MG, Schmidt ML, Lee VM, *et al*. Alpha-synuclein in Lewy bodies [letter]. *Nature* 1997;**388**:839–40.
32 Doty RL, McKeown DA, Lee WW, *et al*. A study of the test-retest reliability of 10 olfactory tests. *Chem Senses* 1995;**20**: 645–56.
33 Nordin S, Murphy C. Odor memory in normal aging and Alzheimer's disease. *Ann N Y Acad Sci* 1998;**855**:686–93.
34 Murphy C, Bacon AW, Bondi MW, *et al*. Apolipoprotein E status is associated with odor identification deficits in non-demented older persons. *Ann N Y Acad Sci* 1998;**855**:744–50.
35 Graves AB, Bowen JD, Rajaram L, *et al*. Impaired olfaction as a marker for cognitive decline: interaction with apolipoprotein E epsilon4 status. *Neurology* 1999;**53**: 1480–7.

## NEUROLOGICAL STAMP

# Vladimir Mikhailovich Bechterev (1857–1927)




Bechterev studied brain stem anatomy (1894) and later as a contemporary of Pavlov contributed to "psychoreflexology" (1900). He achieved a place in Russian neurology nearly equivalent to Pavlov. Bechterev (1885, 1887) added to Dieter's work by distinguishing between the anterior and posterior roots of the eighth nerve. He called the first the *ramus vestibularis* and the second *ramus cochlearis*. He associated the vestibular root with Dieter's nucleus. His work led to a better understanding of some components of the eight nerve that had acoustic functions. In 1894 he also described the nuclear complexes of the reticular formation, connections of the inferior olive, components of the cerebellar peduncles, the central tegmental tract, and the superior vestibular nucleus (nucleus of Bechterev). Bechterev also described the spinothalamic tract (1904) as the pain pathway and contributed to the motor and sensory functions of the brain and the theory of cerebral localisation. In 1909 Bechterev reported that unilateral removal of the inferior colliculus led to transient diminution of reflex movements of the ear contralateral to sounds.

The first association of memory with a specific part of the limbic system seems to have been made by Bechterev. He described in 1900 the brain of a patient with memory deficit and hippocampal degeneration. Bechterev also described ankylosing spondylitis, known for a time as Bechterev's disease.

In 1952 Russia issued a postage stamp commemorating the 25th anniversary of his death. (Stanley Gibbons 1790, Scott 1655)

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