

## Appendix

### **Inclusion criteria**

- a. Papers comparing images of AD patients with NCBCs vs. AD patient without NCBCs, or
- b. Papers comparing images of AD patients with NCBCs vs. normal controls, or
- c. Papers comparing prevalence or degree of severity of NCBCs in AD patients with different imaging results

### **Exclusion criteria**

- a. Reviews
- b. Case reports

### **Imaging methods**

- CT = Computed tomography
- MR = Magnetic resonance
- SPECT = Single photon emission computed tomography
- PET = Positron emission tomography

**Table S1**  
**Results of the systematic review: references identified and reviewed**

	Identified from Medline or PsychInfo (extracted from references)	Relevant based on inclusion/exclusion criteria
Depression	182 (5)	21
Psychosis	117 (0)	34
Apathy	80 (0)	33
Aggression, agitation, hyperactivity	63 (22)	8
Anxiety	41 (2)	9
Sleep disorders	50 (12)	2

**Table S2: Neuroimaging studies in Alzheimer's disease and depression  
Abbreviations for Tables S2A-C:**

**DEPRESSION SCALE**

Dep Scale = Depression Scale

NPI = Neuropsychiatric Inventory

HAM-D = Hamilton Depression Scale

CSDD = Cornell Scale for Depression in Dementia

NIMH AD = National Institute of Mental Health Alzheimer Dementia

DSM-IV = Diagnostic and Statistical Manual, 4<sup>th</sup> edition

MDD = Major Depressive Disorder

MDRS = Mattis Dementia Rating Scale

MMSE = Mini-mental State Examination

NEO-PI = NEO Personality Inventory for current depression

GDS = Geriatric Depression Scale

CES-D = Center for Epidemiologic Studies Depression Scale

ICD = International Statistical Classification of Diseases and Related Health Problems

MADRS = Montgomery Asberg Depression Rating Scale

DDES = Duke Depression Evaluation Scale

**METHOD**

SPECT = Single Photon Emission Computed Tomography

MRI = Magnetic Resonance Imaging

PET = Positron Emission Tomography

FDG-PET = 2-[<sup>18</sup>F]fluoro-2-deoxy-D-glucose (FDG)- Positron Emission Tomography

rCBF = regional Cerebral Blood Flow

fMRI = functional Magnetic Resonance Imaging

**SUBJECTS**

AD = Alzheimer's Disease

FTD = Fronto-temporal Dementia

VaD = Vascular Dementia

LBD = Lewey Body Dementia

**Table S2A**  
**SPECT and PET metabolism studies in Alzheimer's Disease and depression**

<b>Source</b>	<b>Dep Scale</b>	<b>Method</b>	<b>Subjects</b>	<b>Findings</b>
Akiyama et al. 2008	NPI	SPECT	26 AD+depression 18 AD	Depression associated with reduced left dorsolateral prefrontal cortex perfusion
Ebmeier et al. 1997	HAM-D	SPECT MRI	22 AD 40 Late life depression	AD associated with left temporoparietal hypoperfusion, reduced temporal lobe width re: depression: severity of depression symptoms associated with frontal and basal ganglia hypoperfusion
Ebmeier et al. 1998	HAM-D	SPECT	15 AD 18 Late life depression 21 Early onset depression 11 healthy	Late life depression associated with reduced temporal lobe perfusion and periventricular white matter changes re: healthy AD associated with reduced frontal perfusion and deep white matter changes re: healthy.
Galynker et al. 2000	HAM-D	SPECT	25 AD	Depression associated with normal perfusion of frontal and cingulate areas
Kataoka et al. 2010	NPI depression	SPECT	17 AD+depression 18 AD	Depression associated with L callosomarginal segment of L prefrontal cortex hypoperfusion
Levy-Cooperman et al. 2008	CSDD	SPECT	27 AD+depression 29 AD	Depression associated with lower dorsolateral prefrontal cortex and superior prefrontal perfusion
Oshima et al. 2014	NPI depression	SPECT	57 AD	Depression associated with L mid-frontal hypoperfusion
Terada et al. 2014	NPI depression	SPECT	79 AD	Depression associated with L middle frontal gyrus (BA9) hypoperfusion
Holthoff et al. 2005	NPI	PET FDG	26 AD 10 AD+depression 17 AD+apathy	Lower dorsolateral prefrontal cortex metabolism in AD with depression; lower L orbito-frontal metabolism in AD w/ apathy

Lee et al. 2006	NIMH AD depressive syndrome	PET FDG	12 AD+depression 12 AD	Depression associated with lower R sup front gyrus metabolism
Lopez et al. 2001	DSM-IV MDD MDRS MMSE	PET rCBF	5 AD 1 AD+depression 1 AD+emotion lability 1 AD+apathy	1 AD+ depression associated with reduced regional cerebral blood flow anterior cingulate & superior temporal cortex bilateral, L dorsolateral prefrontal cortex, R medial temporal cortex, R parietal cortex; 1 AD+apathy associated with reduced regional cerebral blood flow dorsolateral prefrontal cortex, L basal ganglia; all re: 5 AD.

**Table S2B**  
**Grey and white matter changes in Alzheimer's disease and depression**

<b>Source</b>	<b>Dep Scale</b>	<b>Method</b>	<b>Subjects</b>	<b>Findings</b>
Boccia et al. 2015	Not Assessed	MRI meta-analysis	AD Late life depression	Hippocampus, posterior cingulate atrophy in AD; Hippocampus, frontal, and precuneate atrophy in late life depression
Clark et al. 1998	DSM-III-R MDD; Clinician-rated depression scale sx NEO-PI	MRI	31 AD	Nothing re: MD episodes; Depression symptoms associated with anterior white matter hyperintensities
Ebmeier et al. 1997	HAM-D	SPECT MRI	22 AD 40 Late life depression	AD associated with L temporoparietal hypoperfusion, reduced temporal lobe width re: depression; severity of depression symptoms associated with frontal and basal ganglia hypoperfusion
Elcombe et al. 2015	GDS	MRI	218 w/mood or memory complaints	Depression associated with decreased hippocampal volume
Enache et al. 2015	CSDD or antidepressant use	MRI	57 AD 42 AD+depression	Depression associated with less R medial temporal atrophy
Geerlings et al. 2012	CES-D or antidepressant use	MRI	630 elderly w/o dementia	Depression associated with decreased hippocampal volume, increased white matter hyperintensity.
Hu et al. 2015	NPI depression	MRI	85 AD 131 healthy	Depression associated with L mid-frontal atrophy
Joko et al. 2016	ICD criteria (unspecified)	MRI	58 AD 20 Late life depression 22 healthy	Late life depression associated with decreased hippocampal volume but not as severe as in AD
Lebdev et al. 2013	MADRS	MRI	23 AD+depression 30 AD	Depression associated with prefrontal & temporal thinning; Treatment-associated thinning associated with parahippocampal thinning

Lebdeva et al. 2014	CSDD GDS	MRI	189 AD	Depression associated with L parietal and temporal thinning
Lind et al. 2006	Gottfries-Brane- Steen scale	MRI	67 AD, FTD, VaD, mixed AD+VaD	NS
Meltzer et al. 1999	HAM-D	PET	6 AD 3 AD+depression 11 LLD 10 Controls	No 5-HT <sub>2A</sub> binding potential abnormalities.
Morra et al. 2009	GDS	MRI	189 AD	Depression associated with R hippocampal atrophy
Mueller et al. 2010	DSM-IV MDD	MRI	20 AD 32 VaD or Vascular micro- cerebral infarcts 42 Controls	Depression associated with frontal white matter hyperintensities Cog deterioration associated with grey matter atrophy
O'Brien et al. 1996	MADRS	MRI	61 AD 60 MDD 39 Controls	AD associated with periventricular WMH; MDD associated with deep white matter hyperintensities
O'Brien et al. 2000	MADRS	MRI	28 AD 25 VaD 27 LBD 26 Controls	In all dementia etiologies depression associated with frontal white matter hyperintensities
Pantel et al. 1997	HAM-D MADRS	MRI	19 late life depression 13 Controls	Depression not associated with cortical atrophy; increased ventricle brain ratio suggests central atrophy
Shimoda et al. 2015	HAM-D	MRI	17 late life depression 21 AD	Both AD and late life depression associated with mesial temporal and ant cingulate atrophy; AD only associated with post cingulate and precuneus atrophy
Son et al. 2013	GDS	MRI	14 AD+depression 32 AD	Depression associated with L inferotemporal gyrus atrophy
Starkstein et al. 2009	Depression and Apathy from psych eval.	MRI	79 AD	Depression associated with R parietal white matter hyperintensities; Apathy associated with frontal white matter hyperintensities



Steffens et al. 2002	DDES (Duke depression eval schedule)	MRI	115 Late life depression	Decreased L hippocampal volume associated with later AD
Sturm et al. 2013	GDS	MRI	64 AD 62 MCI 111 Controls	Depression not associated with structural changes
Swann et al. 1997	MADRS	MRI	5 Controls+Hippocampal atrophy 5 Controls- Hippocampal atrophy 7 Depression + Hippocampal atrophy 7 Depression - Hippocampal atrophy 12 AD+ Hippocampal atrophy 12 AD- Hippocampal atrophy	Hippocampal atrophy not associated with later cognitive decline
Taylor et al. 2014	MADRS	MRI	92 LLD 70 Controls	Depression associated with decreased hippocampal volume
Veredelho et al. 2013	GDS	MRI	90 Dementia 147 MCI (from cohort of 639 healthy)	Depression and white matter hyperintensities both associated with later decline
Wu et al. 2006	SCID-IV, HAM-D	MRI	11 Late life depression 8 Controls	Late life depression associated with deep white matter hyperintensities (R anterior thalamus radiation, R uncinate fasciculus, corpus callosum, inferior fronto-occipital)

**Table S2C**  
**Other neuroimaging modalities in Alzheimer's disease and depression**

<b>Source</b>	<b>Dep Scale</b>	<b>Method</b>	<b>Subjects</b>	<b>Findings</b>
Chung et al. 2015 (2016)	GDS NPI depression	PET	153 AD	Depression not associated with cortical amyloid beta
Guo et al. 2015	HAM-D	fMRI	15 AD+depression 17 AD	Depression associated with decreased regional homogeneity in R precentral gyrus, R superior frontal gyrus, R mid-frontal gyrus, R inferior frontal cortex
Tsai et al. 2013	GDS	MRI/MRS	26 AD	Depression associated with increased choline/creatine in L dorsolateral prefrontal cortex and increased myoinositol/creatine in cingulate cortex bilaterally

**Tables 3: Neuroimaging of Alzheimer's disease and psychosis**  
**Abbreviations for Tables 3A – G**

AH = Auditory Hallucinations

BEHAVE-AD = Behavioral Pathology in Alzheimer's Disease

BPSD = behavioral and psychological symptoms of dementia.

CERAD BRSP = Consortium to Establish a Registry for Alzheimer's Disease Behavior Rating Scale for Dementia

CUSPAD = Columbia University Scale for Psychopathology in Alzheimer's Disease

DMI = Delusions of Misidentification

DNOS = Delusions, Not Otherwise Specified

DP = Disintegrative Psychosis

HNOS = Hallucinations, Not Otherwise Specified

NPI = neuropsychological inventory

VH = Visual Hallucinations

**Table S3A**  
**In Vivo Cerebral Atrophy in Patients with Alzheimer's Disease With and without Psychosis**

Source	Behavior (Instr.)	Imaging method	Design	Findings
Barber et al., 2001	DNOS DMI AH VH (CUSPAD)	MR-V	22 AD v 26 C	No assoc. between any psychotic sxs. and any measure of atrophy
Bruen et al., 2008	DNOS	MR	31 preselected for BPSD	DNOS assoc. with ↓ GM density in: a. R inf F gyrus (BA 45) b. R inf P lobule (BA 40) c. L inf F gyrus (BA 45) d. L med F gyrus (BA 11) e. L claustrum
Forstl et al., 1991	DMI	CT	40 AD + P v 88 AD - P	DMI assoc. with larger ant. horn of R lat. vent.
Geroldi et al., 2000	DP (NPI)	CT	19 AD + P v 22 AD - P	DP assoc. with asymmetry (R>L) of T horns.
Geroldi et al., 2002	DP (NPI)	CT	19 AD + P v 22 AD - P	1. DP assoc. with asymmetry (R>L) of T horns 2. DP assoc. with asymmetry (L>R) of F horns
Holroyd et al., 2000	VH	MR	7 AD + P v 7 AD -P	VH assoc. with ↓ O to whole brain ratio
Howanitz et al., 1995	DNOS HNOS	MR	20 AD +P v 12 AD - P	1. HNOS assoc. with: a. Overall atrophy b. R lat. vent. size c. L lat. vent. size 2. No assoc. between HNOS and size of T horns or 3rd vent. 3. No assoc. between DNOS any measure of atrophy

Serra et al., 2010	DNOS HNOS (NPI)	MR-V	27 AD + P v 39 AD - P v 23 C	DNOS assoc. with ↓ grey matter volume in tail of R hippo.
Whitehead et al., 2012	DP (NPI)	MR	23 AD + P v 90 AD - P	<ol style="list-style-type: none"> <li>1. DP in males not assoc. with cortical thickness</li> <li>2. DP in females assoc. with ↓ cortical thickness in: <ol style="list-style-type: none"> <li>a. L F pole</li> <li>b. L med. OFC</li> <li>c. L T pole</li> <li>d. L inf., middle, &amp; sup. T gyri</li> <li>e. R T pole</li> <li>f. R middle &amp; sup. T gyri</li> </ol> </li> </ol>

**Table S3B**  
**In Vivo White Matter Changes in Patients with Alzheimer's Disease with and without Psychosis**

Source	Behavior (Instr.)	Imaging method	Design	Findings
Barber et al., 1999	DNOS VH AH (CUSPAD)	MR	28 AD v 26 C	1. DNOS assoc. with absence of O WMΔ 2. VH assoc. with absence of O WMΔ
Howanitz et al., 1995	DNOS HNOS	MR	20 AD +P v 12 AD - P	1. No assoc. between DNOS and WMΔ 2. No assoc. between HNOS and WMΔ
Lee et al., 2006 **	PNOS DMI DP (CERAD BRSD)	MR	10 AD + P v 45 AD - P	1. DMI assoc. with total WMΔ 2. DMI assoc. with BL F WMΔ 3. DMI assoc. with R P-O WMΔ 3 DMI assoc. with L BG WMΔ
Lin et al., 2006	VH	MR	5 AD + P v 5 AD - P	1. VH assoc. with O periventricular caps 2. VH not assoc. with O deep WMΔ
Lopez et al., 1992	PD HNOS	CT	Prosp: 22 AD + WMΔ v 22 AD - WMΔ	1. At outset: 1 AD + WMΔ had PD; 5 AD - WMΔ had PD; At 1y: 7 AD + WMΔ had PD; 5 AD - WMΔ had PD; neither difference was sig. 2. At outset: 5 AD + WMΔ had HNOS; 5 AD - WMΔ had HNOS; At 1y: 4 AD + WMΔ had HNOS; 6 AD - WMΔ had HNOS; neither difference was sig.
Ogawa et al., 2013	DNOS HNOS (NPI)	MR	93 AD + WMΔ v 70 AD - WMΔ	WMΔ assoc. with ↑ DNOS

Starkstein et al., 1997	DNOS	MR	15 AD + WMΔ v 23 AD – WMΔ	WMΔ not assoc. with DNOS.
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Note. DNOS = Delusions, Not Otherwise Specified; HNOS = Hallucinations, Not Otherwise Specified; AH = auditory hallucinations; VH = visual hallucinations; DMI = Delusions of Misidentification; DP = Disintegrative Psychosis; NPI = neuropsychological inventory; WMΔ = white matter changes .

\*Re. Binetti et al., 1995: Findings re AD are confounded because patients with delusions were not stratified by diagnosis (AD vs. MID)

\*\*Re. Lee et al, 2006: This group also reported associations between specific delusions and WMH.

**Table S3C**  
**In Vivo Cerebral Blood Flow in Patients with Alzheimer's Disease with and without Psychosis**

Source	Behavior	Imaging method	Design	Findings
Fukuhara et al., 2001	DP (theft; NPI)	SPECT ( <sup>99m</sup> Tc-HMPAO)	9 AD + P v 9 AD - P	DP assoc. with ↓ rel. CBF R med. post. P region
Kotrla et al., 1995	DNOS HNOS (BEHAVE-AD)	SPECT ( <sup>99m</sup> Tc-HMPAO)	29 AD + DNOS v 17 AD - DNOS; 10 AD + HNOS v 36 AD - HNOS	1. DNOS assoc. with ↓ rel. CBF L F lobe 2. HNOS assoc. with ↓ rel. CBF BL P lobes 3. HNOS assoc. with ↓ rel. CBF L inf. F lobe
Lee et al., 2009	DNOS (BEHAVE-AD)	SPECT ( <sup>99m</sup> Tc-ECD)	41 AD v 12 C	DNOS assoc. with ↓ rel. CBF BL F lobes
Lopez et al., 2001*	PNOS DNOS HNOS (interview)	<sup>15</sup> O PET	4 AD + P v 5 AD - P	1. PNOS assoc. with ↓ rel. CBF L med T cortex and L DLPFC 2. HNOS assoc. with ↓ rel. CBF R P cortex
Matsuoka et al., 2010	DNOS (NPI)	SPECT ( <sup>123</sup> I-IMP)	14 AD + P v 21 AD - P	DNOS assoc. with ↓ rel. CBF R ant. insula
Mega et al., 2000	PNOS (NPI)	SPECT ( <sup>99m</sup> Tc-HMPAO)	10 AD + P v 10 AD - P	PNOS assoc. with ↓ rel. CBF in: a. L DLPFC (BA 4, 8) b. R DLPFC (BA 4, 6) c. L med. OFC (BA 11) d. R med. F (BA 8) e. L ant CG (BA 32) f. L ventral striatum g. L pulvinar h. L dorsolateral P (BA 40) i. L cerebellum



Moran et al., 2008	PNOS (BEHAVE-AD)	SPECT ( <sup>99m</sup> Tc-HMPAO)	51 AD + P v 52 AD - P	<ol style="list-style-type: none"> <li>1. PNOS in females assoc. with ↓ rel. CBF in:             <ol style="list-style-type: none"> <li>a. R inferolat. F (BA 10)</li> <li>b. R inf. T (BA 20)</li> </ol> </li> <li>2. PNOS in males assoc. with ↑ rel. CBF in R striatum</li> <li>3. PNOS in males assoc. with ↓ rel. CBF in:             <ol style="list-style-type: none"> <li>a. B/L med. F (BA 10)</li> <li>b. R sup. F (BA 8)</li> <li>c. R P (BA 7)</li> <li>d. L O (BA 18)</li> </ol> </li> </ol>
Nakano et al., 2006	DNOS (NPI)	SPECT ( <sup>99m</sup> Tc-ECD)	25 AD + P v 39 AD - P v 76 C	<ol style="list-style-type: none"> <li>1. AD + DNOS v controls: DNOS assoc. with ↓ rel. CBF in B/L F lobes</li> <li>2. AD + DNOS v AD - DNOS: DNOS assoc. with ↓ rel. CBF in:             <ol style="list-style-type: none"> <li>a. R PFC</li> <li>b. R inf. to middle T cortex</li> <li>c. R inf P lobule</li> </ol> </li> </ol>
Nakatsuka et al., 2013	DNOS (BEHAVE-AD)	SPECT ( <sup>99m</sup> Tc-ECD)	27 AD + P v 33 AD - P	<ol style="list-style-type: none"> <li>1. D of theft assoc. with ↓ rel. CBF in:             <ol style="list-style-type: none"> <li>a. B/L T poles</li> <li>b. R inf. T gyrus</li> </ol> </li> <li>2. Suspiciousness assoc. ↓ rel. CBF in B/L T poles</li> <li>3. D of abandonment assoc. with ↓ rel. CBF in:             <ol style="list-style-type: none"> <li>a. R para hippo. gyrus</li> <li>b. R Post. insula</li> </ol> </li> <li>4. D "house not home" assoc. with ↓ rel. CBF in R amygdala</li> </ol>

Nomura et al., 2012 **	DNOS (NPI)	SPECT ( <sup>123</sup> I-IMP)	25 AD + P (preselected)	<ol style="list-style-type: none"> <li>1. "Factor1" (House not home; people not who they claim to be; phantom boarder; abandonment) assoc. with: <ol style="list-style-type: none"> <li>a. ↓ rel. CBF in R middle T gyrus</li> <li>b. ↑ rel. CBF in L med. F gyrus (BA 6), L precentral gyrus (BA 4)</li> </ol> </li> <li>2. "Factor2" (TV sign, persecution) assoc. with: <ol style="list-style-type: none"> <li>a. ↓ rel. CBF in B/L precuneus (BA 31, 7)</li> <li>b. ↑ rel. CBF in L insula, R TH, R F subgyrus</li> </ol> </li> <li>3. "Factor 3" (abandonment and jealousy) assoc. with: <ol style="list-style-type: none"> <li>a. ↓ rel. CBF in R inf. T (BA 20), R inf. F (BA 10)</li> <li>b. ↑ rel. CBF in L middle F gyrus, L insula, L putamen, L post. CG (BA31)</li> </ol> </li> </ol>
Ponton et al., 1995 ***	DNOS (NR)	SPECT ( <sup>99m</sup> Tc-HMPAO & <sup>133</sup> Xe)	15 AD - P	<ol style="list-style-type: none"> <li>1. Baseline: DNOS assoc. with ↓ rel. CBF in: <ol style="list-style-type: none"> <li>a. B/L sup. T gyrus (BA 19)</li> <li>b. R inf. T gyrus</li> </ol> </li> <li>2. At 1 y: DNOS not assoc. with CBF</li> </ol>
Staff et al., 1999	DNOS (semi-structured assessment)	SPECT ( <sup>99m</sup> Tc-HMPAO)	18 AD + P v 15 AD - P	ROI analysis: DNOS assoc. with ↓ rel. CBF in R F, P, T & "limbic" lobes
Staff et al., 2000 ****	DNOS	SPECT ( <sup>99m</sup> Tc-HMPAO)	10 AD + CSAD v 15 AD + NCSAD v 20 AD - P see footnote	SPM analysis: <ol style="list-style-type: none"> <li>a. CSAD v AD - P: CSAD assoc. with ↓ rel. CBF in R F (Part of BA 9)</li> <li>b. CSAD v AD + NCSAD: CSAD assoc. with ↓ rel. CBF in R F (Part of BA 9)</li> </ol>
Starkstein et al., 1994	DNOS	SPECT ( <sup>99m</sup> Tc-HMPAO)	16 AD + P v 29 AD - P	DNOS assoc. with ↓ rel. CBF in B/L inf. and sup. T lobes
Starkstein et al., 1997	DNOS (Dementia Psychosis Scale)	SPECT ( <sup>99m</sup> Tc-HMPAO)	15 AD + WMΔ v 23 AD - WMΔ	CBF not assoc. with DNOS.

\*Re. Lopez et al., 2001: One pt. with DNOS had ↑rel CBF in R TH, the other had ↑rel CBF in L TH. One pt with HNOS had ↑rel CBF in R BG and TH; the other pt. with HNOS had ↑rel CBF in R ant. CG, R OFC, and B/L BG.

\*\*Re. Nomura et al, 2012: This study is unique (and not actually controlled) in having started with preselected delusional AD patients, divided them according to novel delusional "types" determined by factor analysis, and comparing CBF between those delusional types.

\*\*\*Re. Ponton et al., 1995: Prospective longitudinal study with 1 y follow-up. None of the subjects had delusions at the outset. 6 developed delusions.

"Baseline" findings for the delusional subgroup are retrospective.

\*\*\*\*Re. Staff et al., 2000: The 45 AD subjects included 10 with the content specific autobiographical delusion that a family member was still alive (CSAD); 15 with other delusions (NCSAD), and 20 without delusions.

**Table S3D**  
**In Vivo Cerebral Metabolism in Patients with Alzheimer's Disease with and without Psychosis**

Source	Behavior	Imaging method	Design	Findings
Hirono et al., 1998	DNOS (BPADRS or NPI)	<sup>18</sup> FDG PET	26 AD + P v 39 - P	1. DNOS assoc. with ↑ CMRglu in L ant. T gyrus 2. DNOS assoc. with ↓ CMRglu in L med. O region
Mentis et al., 1995	DMI	<sup>18</sup> FDG PET	9 AD + P v 15 - P v 17 C	1. ROI data: DMI assoc. with ↓ CMRglu in: a. B/L OFC b. L post. med. T c. L ant. CG d. B/L post CG e. L caudate nuc f. L lentiform nuc L calcarine 2. Statistical parametric mapping data: DMI assoc. with ↓ CMRglu in: a. B/L OFC b. B/L ant. CG (BA 10, 11, 32, 25) DMI assoc. with ↑ CMRglu in: a. B/L sup. T b. B/L inf. P c. B/L precuneus
Sultzer et al., 1995 *	PNOS	<sup>18</sup> FDG PET	21 AD see footnote	PNOS assoc. with ↓ CMRglu in B/L F lobes
Note. DNOS = Delusions, Not Otherwise Specified; BPADRS = Behavioral Pathology in Alzheimer's Disease Rating Scale; NPI = neuropsychological inventory; DMI = Delusions of Misidentification;				

\* Re. Sultzer et al., 1995: This study does not report how many subjects exhibited psychosis. It reports correlations between psychosis scores and metabolism.

**Table S3E**  
**Other imaging studies in Patients with Alzheimer's Disease With and without Psychosis**

<b>Source</b>	<b>Behavior</b>	<b>Imaging method</b>	<b>Design</b>	<b>Findings</b>
Forstl et al., 1992b	DNOS (interview)	CT	5 AD with BGM vs 5 AD without	DNOS assoc. with BGM
Reeves et al., 2009	DNOS (NPI)	[ <sup>11</sup> C]raclopride [RAC] PET	7 AD +P v 16 AD - P	DNOS assoc. with ↑ [ <sup>11</sup> C]RAC BPND (binding potential of striatal DA D2/D3 receptors)
Shinno et al., 2007	DNOS (BEHAVE-AD)	<sup>1</sup> H MRS	8 AD +P v 22 AD - P	1. DNOS assoc. with ↓ NAA/Cr in ant. CG 2. DNOS assoc. with ↑ mI/Cr in ant. CG

**Table 4: Neuroimaging of Alzheimer's disease and anxiety  
Abbreviations for Table 4**

**BEHAVIOR**

NPI = Neuropsychiatric Inventory

BPSD = Behavioral and Psychological Symptoms of Dementia

MMSE = Mini-mental State Examination

OCD = Obsessive Compulsive Disorder

**METHOD**

MRI = Magnetic Resonance Imaging

PET = Positron Emission Tomography

FDG-PET = 2-[<sup>18</sup>F]fluoro-2-deoxy-D-glucose (FDG)- Positron Emission Tomography

SPECT = Single Photon Emission Computed Tomography

WMH = White Matter Intensities

**DESIGN**

AD = Alzheimer's Disease

**Table 4:**  
**Neuroimaging studies of in Patients with Anxiety and Alzheimer's Disease**

<b>Source</b>	<b>Behavior</b>	<b>Method</b>	<b>Design</b>	<b>Findings</b>
Berlow et al. 2010	NPI anxiety Other BPSD MMSE	MRI WMH volume	37 AD	WMH volume associated with NPI anxiety and other BPSD
Hashimoto et al., 2006	NPI anxiety (frequency x severity)	18 FDG PET	41 AD	Anxiety associated with lower metabolism in bilateral entorhinal cortex, anterior parahippocampal gurus, left superior temporal gyrus, left insula.
Horenik et al., 2006	NPI anxiety MMSE	MRI	27 AD 15 healthy controls	No correlation of amygdala volume with NPI anxiety (or any other NPI score) MMSE score correlated with absolute amygdala volume
Marksteiner et al., 2003	OCD	MRI SPECT	1 AD 5 healthy controls	Cerebral atrophy esp. temporal lobes, reduced temporal lobe rCBF
Poulin et al., 2011	NPI anxiety	MRI	174 AD 193 healthy controls	Amygdala atrophy not significantly related to NPI anxiety
Serra et al., 2010	NPI anxiety	MRI	19 aMCI 15 early AD 12 moderate AD 23 healthy controls	Anxiety unrelated to gray matter atrophy anywhere in the brain
Sultzer et al., 1995	Neurobehavioral Rating Scale Anxiety/ Depression factor score	18 FDG PET	21 AD	Anxiety/Depression factor score related to parietal lobe hypometabolism

## Ovid MEDLINE Pilot Search Algorithms and Results

(aggression.mp. or exp Aggression/)+ (Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 13 citations

agitation.mp. + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 14 citations

(exp Anxiety/ or anxiety.mp.) + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 41 citations

(apathy.mp. or exp Apathy/) + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 53 citations

(exp Depression/ or depression.mp.) + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 211 citations

Note: since the term “depression” has many meanings in medical science, we determined that this search algorithm overestimated the pertinent literature. The search was repeated adding the qualifier AND (mood.mp or mood disorder.mp. or exp Mood Disorders/)

Result = 75 citations

(euphoria.mp. or exp Euphoria/ or mania.mp.) + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 2 citations



hyperactivity.mp. + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 18 citations

(exp Psychotic Disorders/ or psychosis.mp.) + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 25 citations

(exp Wandering Behavior/ or wandering.mp.) + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 3 citations

(exp Sleep/ or sleep.mp. or sleep disorder.mp. or exp Sleep Disorders/) + (exp Alzheimer Disease/ or alzheimers.mp.) + (exp Magnetic Resonance Imaging/ or exp Tomography, X-Ray Computed/ or computed tomography.mp. or exp Positron-Emission Tomography/ or exp Tomography, Emission-Computed, Single-Photon/ or exp Magnetic Resonance Spectroscopy/)

Result = 34 citations