Regional brain abnormalities in behavioral variant frontotemporal dementia: a meta-analysis

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Abstract

INTRODUCTION: Numerous studies have reported brain alterations in behavioral variant frontotemporal dementia (bvFTD). However, they pointed to inconsistent findings.

METHODS: We used a meta-analytic approach to identify the convergent structural and functional brain abnormalities in bvFTD. Following the best-practice neuroimaging meta-analysis guidelines, we searched PubMed and Embase databases and performed reference tracking. Then, the coordinates of group comparisons between bvFTD and controls from 73 studies were extracted and tested for convergence using activation likelihood estimation.

RESULTS: We identified convergent abnormalities in the anterior cingulate cortices, anterior insula, amygdala, paracingulate, striatum, and hippocampus. Task-based and resting-state functional connectivity pointed to the joint networks that are connected to the obtained consistent regions. Functional decoding analyses suggested associated dysfunction of emotional processing, interoception, reward processing, higher-order cognitive functions, olfactory and gustatory perceptions in bvFTD.

DISCUSSION: Our findings highlighted a key role of the salience network and subcortical regions in the pathophysiology of bvFTD.

Keywords: Behavioral Variant Frontotemporal Dementia; Activation Likelihood Estimation; Voxel-Based Morphometry; Positron Emission Tomography; Functional Magnetic Resonance Imaging.

1. Introduction

Behavioral-variant frontotemporal dementia (bvFTD) is a neurodegenerative syndrome characterized by neurodegeneration in the frontal and anterior temporal lobes leading to insidious and progressive changes in behavior, personality and social functions [1]. BvFTD is the most common frontotemporal dementia (FTD) syndrome and the second major cause of early-onset dementia after Alzheimer's disease (AD). The prevalence of bvFTD is estimated to be approximately 13/100,000 with at sixties which is the peak age of onset of bvFTD [1]. Given the heterogeneous symptomology and gradual course of bvFTD, early detection of bvFTD is often abstruse and causes frustrating experiences for patients and relatives [2]. Around 50% of patients are initially misdiagnosed with psychiatric disorders due to the overlapping behavioral symptoms and in later stages with AD due to cognitive impairments. Recently, diagnostic accuracy of bvFTD has been improved dramatically by introducing the consensus clinical criteria that rely on a hybrid approach incorporating clinical symptoms and neuropsychological assessment for "possible bvFTD", additional neuroimaging testing and cognitive decline evaluation for "probable bvFTD", and further neuropathology and genetic confirmation for "definite bvFTD" [3]. Thus, nowadays, neuroimaging is an essential step for bvFTD diagnosis.

Numerous neuroimaging studies identified structural and functional brain alterations in patients with bvFTD. In particular, structural magnetic resonance imaging (MRI) techniques including Voxel-Based Morphometry (VBM) have provided collective evidence for regional brain atrophy predominantly in the frontal and anterior temporal lobes, insula, anterior cingulate and several subcortical structures including the amygdala, hippocampus, striatum, putamen, thalamus, caudate and hypothalamus [4]. As such, presence of pathological atrophy in the frontotemporal regions is one of the diagnostic criteria of "probable" bvFTD. However, its neuroanatomical assessment in the initial stages is often insufficient due to gradual occurrence of brain atrophy. Functional imaging techniques such as functional MRI (fMRI) and fluorodeoxyglucose positron emission tomography (FDG-PET) usually provide a higher sensitivity to detect brain dysfunctions before the emergence of clinical symptoms [5]. The most observed structural and functional brain changes in early stages of bvFTD target a group of interconnected brain regions, so-called "salience network" (SN), which is associated with social-emotional processing [1]. Taken together, integrating structural and functional brain alterations in bvFTD may increase accuracy of neuroimaging biomarkers and may improve the specificity

of probable bvFTD criteria. However, the individual neuroimaging studies in bvFTD point to divergent findings due to heterogeneous clinical samples, diversity of imaging modalities, flexible analyses and statistical methods. Thus, a consolidation of the literature is needed to overcome the previous inconsistencies. Quantitative assessment of neural abnormalities using neuroimaging meta-analysis is a favorable tool to overcome such divergence in the bvFTD literature [6, 7]. There are few previous bvFTD neuroimaging meta-analyses that indicated atrophy and hypometabolism in a wide number of brain regions covering the frontomedial cortex, basal ganglia, anterior insula, and the temporal cortex [8-10]. However, these previous meta-analyses were mostly unimodal i.e., including only VBM experiments, FDG-PET, or resting-state fMRI (rs-fMRI) [8-10], included a low number of patients, various selection criteria, and often used liberal statistical methods (e.g., FDR), which provides a significant error to control for false positive results [11].

Using the best-practice neuroimaging meta-analysis guidelines [6, 7], the present study aimed to revisit the past meta-analytic findings by including multimodal datasets including structural MRI, FDG-PET, and fMRI imaging modalities. In order to elucidate consensus structural and functional regional aberrations in bvFTD, we applied activation likelihood estimation (ALE) meta-analysis based on the largest number of individual bvFTD findings. ALE is the most common applied algorithm among the coordinate-based meta-analysis (CBMA) methods which assess the regional convergence between foci obtained from group comparison experiments [12]. Afterward, we located their brain co-activation patterns using meta-analytic co-activation mapping (MACM) [13] and resting-state functional connectivity (RSFC) [14] to reveal the networks connected to the meta-analytic obtained regions. We performed both analyses since MACM reveals the co-activation pattern of various regions in task-based experiments, while RSFC demonstrates the functional connectivity (FC) of each region in resting-state fMRI. Moreover, we performed hierarchical clustering analysis based on their pairwise RSFC profile and functional decoding of the convergent clusters to reveal the sub-networks between convergent regions and assess the functions associated with these regions, respectively. Finally, we assessed functional characteristics of the identified regions using the BrainMap dataset [15].

2. Methods

The present large-scale CBMA was performed following the recently developed best-practice guidelines for neuroimaging meta-analyses [6, 7] and adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16]. The protocol for this study was pre-registered based on the International Prospective Register of Systematic Reviews (PROSPERO, code: CRD42020127902).

2.1. Search and Study Selection

We searched PubMed and Embase databases to retrieve potentially relevant studies in May 2020 using the following keywords: (behavioral variant frontotemporal dementia OR bvFTD OR frontal variant frontotemporal dementia OR frontotemporal dementia OR picks disease) AND (functional magnetic resonance imaging OR fMRI OR voxel-based morphometry OR VBM OR positron emission tomography OR PET). To avoid missing any additional relevant studies, we also traced the references of the included studies and previous reviews/meta-analyses on bvFTD. After removing the duplicates, unique records were independently reviewed by two authors (A.K. & M.M.), first by screening the abstracts and then, for the possible relevant ones, by reading their full-texts. In case of discordance between two raters, the disagreement was settled by another expert reviewer (T.K.). Studies were included if they met the following eligibility criteria: (1) were reported in a peer-reviewed original article and not as a conference abstract; (2) were included bvFTD patients who were clinically diagnosed using the most reliable guidelines at the time of publication [3, 17] and compared them with healthy controls (HC); (3) both bvFTD and control groups were free of any additional major comorbidities such as amyotrophic lateral sclerosis or other neurological disorders; (4) each group was included with $\geq$ six participants; (5) neuroimaging methods including VBM, fMRI (resting-state or task-based), and FDG-PET were used; (6) the analysis had to be whole-brain and not limited to a region of interest (ROI) or seed-based FC; and (7) the results of between-group contrasts were reported as peak coordinates in a standard space (i.e., Montreal Neurological Institute [MNI] or Talairach), or were provided by authors upon our request, in case they were not mentioned in the individual studies.

2.2. Data Extraction

Three independent authors (T.K. & A.K. & M.M.) reviewed the full-texts of the included studies and extracted their relevant data, including bibliographic information, average age and years of education, type of imaging modality (VBM, FDG-PET, rs-fMRI, task-based fMRI (t-fMRI)), and the peak coordinates (x, y, z) of each experiment in MNI or Talairach space. Of note, in CBMA, “experiments” refers to the individual group comparison contrasts (e.g., bvFTD > HC, and HC > bvFTD) reported in a “study”, which indicates an individual publication [6]. Prior to analyses, we transformed Talairach coordinates into the MNI space for all coordinates to set them in the same reference space[18]. In order to avoid pooling the data from overlapping samples, which would potentially influence the results, we identified publications with partially/fully overlapping samples, and merged their data to minimize the within-group effect, as suggested previously [19].

2.3. Activation likelihood estimation analysis

We used the revised version of the ALE method as implemented in MATLAB to test the spatial convergence of the reported coordinates, against the null hypothesis of randomly distributed findings across the brain [12]. In this approach, for each experiment the foci are modeled as 3D Gaussian kernels representing the uncertainty about the location of peak coordinate. The uncertainty is assumed to be greater for experiments with smaller sample sizes, which is characterized by a higher full width at half maximum (FWHM) of Gaussian kernels. Subsequently, a “modeled activation” (MA) map is created for each experiment by combining all of their convolved foci. Next, taking the union of MA maps for all of the included experiments results in an ALE score map, which represents voxel-wise likelihood of convergent findings at each particular brain location. Finally, to distinguish true convergence from random overlap, the ALE score map is statistically tested against a null-distribution of randomly distributed findings [12, 19], at $p < 0.05$ cluster level family-wise error (cFWE) corrected for multiple comparisons.

The experiments were further categorized by their effect direction (in-/decreases) and imaging modalities, and then separate ALE meta-analyses were performed on four subsets of the experiments, which included the minimum required number of experiments for sufficient power (≥ 15) [11]. Our analyses included (i) all the experiments together, (ii) experiments reporting decreases in activity/connectivity, metabolism or grey matter volume (HC > bvFTD), (iii) VBM

experiments, and (iv) combination of functional imaging (FDG-PET, rs-fMRI, t-fMRI) experiments. The other sets of experiments were less than 15 and thus, no analysis was conducted based on them.

2.4. Meta-analytic co-activation mapping

To characterize task-based functional connectivity patterns of the identified convergent brain regions in the all-effects ALE analysis, we used MACM [13]. In this approach, we used the data curated in the BrainMap database [15] derived from more than 10,000 task-based functional neuroimaging studies on healthy individuals, to meta-analytically identify regions that are co-activated across a range of different tasks with the seed region. More specifically, whole-brain peak coordinates of all studies that reported at least one focus of activation within the respective seeds were analyzed using the ALE algorithm and thresholded at $p < 0.05$, FWE cluster-level corrected (voxel-wise, cluster-forming threshold: $p < 0.001$) to detect co-activations areas with the meta-analytic identified regions.

2.5. Resting-state functional connectivity analysis

We also investigated the task-free FC patterns of the convergent meta-analytic clusters using RSFC analysis. Here, the data from 192 healthy individuals obtained from the Enhanced Nathan Kline Institute – Rockland Sample was used [20]. BOLD images were acquired using a Siemens TimTrio 3 T scanner (gradient-echo EPI pulse sequence, TR = 1.4 s, TE = 30 ms, flip angle = 65°, voxel size = 2.0 mm × 2.0 mm × 2.0 mm, 64 slices) while the subjects were in a resting condition and instructed to keep their eyes open. The physiological and movement artifacts were removed from the images using FMRIB's ICA-based Xnoiseifier (version 1.061, as a component of FSL 5.0.9) [21], and additional preprocessing was performed using SPM8 (Wellcome Trust Centre for Neuroimaging, London) and in-house MATLAB scripts, following previously employed processing procedures [22]. To estimate RSFC, Pearson's correlation coefficients of the average time-course of each seed with the time-series of all other gray-matter voxels was calculated and then transformed into Fisher's z scores, which were entered in a second-level ANOVA for group analysis in which age and gender were included as covariates of no-interest. Finally, non-parametric permutation testing was performed to threshold the obtained RSFC maps at $p < 0.05$, FWE corrected for multiple comparisons on the cluster level.

2.6. Overlap of task-based and task-free functional connectivity

The maps of task-based (i.e., MACM) and task-free (i.e., RSFC) connectivity for each seed region were overlapped to estimate their consensus connectivity map and identify the areas that show robust task-independent as well as task-dependent FC. In particular, we performed conjunction analysis across the MACM and RSFC maps [23].

2.7. Anatomical labeling and visualization

To identify the macrostructural label and cytoarchitectural characteristics of the respective brain regions identified in the ALE or functional connectivity analyses, we used the SPM Anatomy Toolbox, V3 [24]. We used MRICroGL v 1.2.2 [25] for brain visualizations.

2.8. Hierarchical cluster analysis

We performed hierarchical clustering based on the pairwise RSFC patterns of identified meta-analytic regions to group them into clusters that contain regions that are as homogenous as possible while maximally distinct from other clusters. To calculate the RSFC matrix, partial temporal correlation between the time series data of all regions was estimated in FSLNets toolbox (<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLNets>) [26], followed by Fisher's z-transformation of correlation coefficients for each pairwise connection which were submitted to one-sample t-tests. The resulting t values, reflecting connection strength, as well as consistency across the samples, were z-transformed into units of the standard normal distribution. The obtained RSFC matrix was then fed into the Ward hierarchical clustering. Of note, to preserve the full pattern of connectivity profiles, all features entered the analyses without any thresholding for significance. Hierarchical clustering was performed through an agglomerative approach in which clusters initially formed by individual regions are subsequently merged according to their similarity using standardized Euclidean distances and Ward's incremental sum of squares method [27].

2.9. Functional decoding analysis

The behavioral domains (BD) of the experiments included in BrainMap database and their associated activation maps were used to explore the functional role of the identified convergent regions [28]. More specifically, within each convergent brain region, the overall a priori chance

of finding activations across all BDs, $P(\text{Activation})$, was compared with the probability of its activation during each particular BD, $P(\text{Activation} \mid \text{BD})$, using binomial tests which were corrected for multiple comparisons using the false discovery rate (FDR), and BDs with a significantly higher probability of activating each respective region than average were reported.

3. Results

3.1. Experiments included in the meta-analysis

After removing duplicate records, we screened 5,047 abstracts and included 73 studies in our meta-analysis (Figure 1, Supplementary Table 1). Of note, among these included papers, 27 studies were performed based on the FRONTIER open dataset and thus, their data were merged to minimize the within-group effect [6]. In addition, eight other studies had partially overlapping samples, and they were pooled together as well. Finally, 31 independent experiments (out of 73 studies) comprising 1672 bvFTD patients and 3884 HC participants were used for ALE analysis. These experiments include VBM ($N = 20$), t-fMRI ($N = 1$), rs-fMRI ($N = 2$) or FDG-PET ($N = 12$). Of note, some experiments used more than one imaging modality; therefore, the collective number of experiments included in each imaging modality exceeds the number of total experiments. Overall, patients and controls had a comparable average age and years of education. Decrease in functional/structural experiments (HC > bvFTD) was observed more commonly ($N = 28$) and only a few studies ($N = 3$) had reported increased functional/structural experiments (bvFTD > HC). The excluded studies during reading full papers and the reasons of exclusion are reported in Supplementary Table 2.

3.2. Convergent regional abnormalities in bvFTD

Firstly, we assessed the consistent structural and functional abnormalities by pooling all experiments ($N = 31$), and identified five convergent clusters in the following regions ($p < 0.05$, cFWE) (Supplementary Table 1, Figure 2A): (i) the right amygdala and hippocampus (max coordinate: 24, -6, -14; 240 voxels), with 17.8% located in CA1, 13.1% in centromedial amygdala, 11.1% in dentate gyrus, 11.4% in ventromedial amygdala, and 7.7% in basolateral amygdala. Convergence in this cluster was mostly driven by VBM experiments (87.8%); (ii) the left caudate and subcallosal cortex (max coordinates: -4, 12, -12; 534 voxels) and area s24 (5.8% voxels), including regions in area 25 (13.8%), area 33 (8.3%), area Fo2 (4.8). Experiments

using VBM (54.6%), FDG-PET (28.5%), or both VBM and FDG-PET (16.8%) contributed to determine this cluster; (iii) bilateral paracingulate gyrus and anterior cingulate cortex (ACC) (max coordinates: 10, 34, 28; 400 voxels), with 14.1% of its volume located in area 24c, 11.4% in area p32, 10.4% in area p24ab, and 2.6% in area 33. Convergence in this cluster was driven by VBM (53.8%), FDG-PET (33.6%), both VBM and rs-fMRI (7.3%), or both VBM and FDG-PET (5.1%) experiments; (iv) bilateral paracingulate gyrus extending to small portions of the medial orbitofrontal cortex (max coordinates: 0, 36, -10; 163 voxels), with 52.5% located in area s32, 2.19% in area s24, 8.9% in area p24ab, and 3.6% in area p32. This cluster almost entirely resulted from the convergence of VBM experiments (98.5%), with only 1.3% contribution of FDG-PET experiments; (v) the left anterior insular cortex (AIC) extending to frontal orbital cortex (max coordinates: -32, 22, 4; 173 voxels), with 30.9% located in area Id6, 29.9% in area Id7, and 9.6% in area OP8. In this cluster the highest contribution was from VBM experiments (72.3%), but FDG-PET experiments also contributed to identify this cluster (27.2%). As most of the included experiments had reported decrease contrasts (HC > bvFTD), performing ALE analysis on these experiments only showed very similar convergent clusters ($p < 0.05$, cFWE) (Supplementary Table 1, Figure 2B).

Next, we performed separate ALE analyses based on imaging modality using VBM ($N = 21$) or combination of functional imaging ($N = 17$) experiments. The ALE analysis on VBM experiments revealed clusters of convergence in the amygdala and hippocampus (max coordinates: 24, -6, -14; 304 voxels), paracingulate gyrus and frontal medial cortex (max coordinates: 0, 36, -10; 203 voxels), as well as the AIC and frontal orbital cortex (max coordinates: -32, 22, 4; 100 voxels) ($p < 0.05$, cFWE) (Supplementary Table 1, Figure 2C). The location of these clusters corresponded to the first, third and fifth clusters of the all-experiments analysis, respectively, but was smaller in size. Confining the analysis to the functional experiments (i.e., FDG-PET, rs-fMRI, and t-fMRI) demonstrated three significant clusters in the left caudate and accumbens (max coordinates: -8 10 0; 276 voxels), paracingulate gyrus and ACC (max coordinates: 10 34 26; 296 voxels), and another more rostral region in the ACC (max coordinates: 4 14 34; 156 voxels). The last cluster, unlike the other two did not correspond to any of the regions identified in the all-experiments analysis. Convergence in the significant clusters of functional analysis was mainly driven by FDG-PET (67.1%-100% contribution) and rs-fMRI

experiments (11.1%-32.9%), while t-fMRI experiments had no contribution ($p < 0.05$, cFWE) (Supplementary Table 1, Figure 2C).

3.3. Connectivity patterns of the identified convergent regions

MACM and RSFC analyses pointed to the joint networks that are connected to the obtained consistent regions (Figure 3, Supplementary Figures 1 and 2). The overlap of MACM and RSFC maps revealed significant task-based and task-free co-activation of the amygdala and hippocampus with the striatum, thalamus, fusiform gyrus, inferior frontal gyrus, and midline frontal regions. MACM analysis demonstrated that this region has significant co-activation with the AIC. In addition, RSFC analysis showed additional task-free connectivity of this region with the entorhinal cortex, superior and middle temporal gyri, precuneus, posterior cingulate cortex, and cerebellum.

The convergent cluster in the left caudate and subcallosal cortex was associated with the striatum, thalamus, AIC, midline frontal regions, posterior cingulate gyrus, and cerebellum in both MACM and RSFC analyses, but with the superior lateral occipital cortex, and middle temporal gyrus only in task-free analysis, and the left superior parietal lobule and parietal operculum only in task-based analysis. The rostral paracingulate and frontal medial cortex cluster showed task-based coactivation and RSFC with the medial frontal regions, posterior cingulate cortex, precuneus, hippocampus, amygdala, and superior lateral occipital cortex, but was also functionally connected to the medial thalamus, AIC, Heschl's gyrus, and cerebellum only in RSFC analysis. Most of the significant regions for this cluster in the MACM analysis were also observed in the RSFC analysis.

The more caudal significant cluster in the paracingulate and ACC similarly functionally connected to the medial frontal regions, AIC, striatum, thalamus, middle and inferior frontal gyri, and posterior cingulate cortex in MACM and RSFC analyses, but additionally revealed RSFC with the cerebellum, and meta-analytic co-activation with the superior parietal lobule and right angular gyrus. The AIC cluster was functionally connected with the paracingulate gyrus and ACC, striatum, thalamus, middle and inferior frontal gyri, superior parietal lobule, and different regions within the cerebellum during both task and rest. In addition, the AIC showed only task-based functional connectivity with the precentral gyrus, fusiform gyrus, and superior parietal

lobule, and RSFC with the temporal pole, Heschl's gyrus, intracalcarine cortex, and lingual gyrus. All these results were corrected for cFWE.

3.4. Hierarchical clustering of convergent findings

To identify functionally coherent sub-networks of the identified consistent regions, we performed hierarchical clustering analysis based on their pairwise RSFC profile. In this analysis, at the first level, we identified two main sub-networks, namely the insula-amygdala network, and the cingulo-striatal network including the ACC, paracingulate cortex, frontal medial cortex, subcallosal cortex, and striatum. The latter was grouped into two additional sub-networks at the second level: one including the two clusters located in the medial frontal lobe, and the other one including the convergent cluster in the striatum and subcallosal cortex (Figure 4).

3.5. Functional decoding of convergent clusters

Our forward-inference functional decoding of the identified regions using the BrainMap database demonstrated their significant involvement in emotional processing, interoception, reward processing, higher-order cognitive functions, as well as olfactory and gustatory perception (Figure 5). More specifically, the amygdala/hippocampus cluster was activated in olfactory perception, processing of negative and positive emotions, and reward processing. The convergent cluster in the left caudate and subcallosal cortex was mostly associated with reward processing, gustatory perception, cognitive reasoning, and sexual interoception. Gustatory perception and reward processing were also associated with the activations in the rostral paracingulate gyrus / frontal medial cortex cluster. The more caudal paracingulate gyrus and the ACC cluster was more likely to be activated in cognitive reasoning and response to rewards. Finally, the AIC was associated with thermal interoception, processing of disgust, and language semantics. All these results were corrected for FDR.

4. Discussion

We performed a large-scale CBMA on both structural and functional brain studies on bvFTD, nearly a decade after the revision of its diagnostic criteria, and found consistent abnormalities in the five clusters including the AIC, ACC, paracingulate cortex, subcallosal cortex, striatum, amygdala, and anterior hippocampus in patients with bvFTD compared to healthy subjects.

These regions predominantly showed decreased grey matter volume, functional hypoactivation, or dysconnectivity, to various degrees in each region. While the abnormalities in the striatum were mainly functional, structural abnormalities were more predominant in the AIC, amygdala, and anterior hippocampus, and midline frontal regions were both functionally and structurally impaired. In addition, we used MACM and RSFC analyses to characterize the connectivity pattern of the convergent regions and observed significant co-activation of them with each other, and with additional brain regions including the thalamus, lateral prefrontal cortex, and association cortices in the parietal lobe. Next, using hierarchical clustering of the convergent regions, we classified them into two main groups: one including the AIC, amygdala, and hippocampus, and the other one including the midline frontal areas and striatum. Moreover, functional decoding analysis showed involvement of the former first set of regions in emotional processing, and of the latter in reward processing and higher-order cognitive functions.

4.1. The key role of the salience network in bvFTD

The cortical layer 5b of AIC and pregenual ACC (pgACC) contains a specialized type of large spindle-shaped projection neurons called von Economo neurons (VEN), which are presumed to be involved in social cognition and self-awareness [29]. The number of these neurons in the AIC and pgACC is significantly depleted in patients with bvFTD [30-32], parallel to clinical severity of bvFTD, and even in the absence of gross atrophy of these regions [29]. Accordingly, histopathological and imaging studies have suggested that the AIC and pgACC are among the earliest atrophied regions in bvFTD [33]. These regions are the key hubs of the SN, which guides behavior in response to the perceived salience of current external/internal events, i.e., their significance for the survival of the individuals [32]. In this network, the AIC and pgACC play distinct, but interdependent roles, acting as afferent (“sensory”) and efferent (“motor”) hubs of the SN, respectively. More specifically, the AIC detects and represents subjective emotional, homeostatic, social, and motivational salience of the immediate environmental or bodily states [34, 35], and the ACC initiates goal-directed behaviors in response to these salient stimuli [36]. Several studies have reported decreased FC within the SN in patients with bvFTD [37]. It is well-documented that the main hubs of the SN can lead to the main characteristic symptoms of bvFTD, including impaired emotional processing and social cognition, disinhibition, executive dysfunction, and apathy.

Impaired emotional recognition is a common symptom in bvFTD and has been reported for different types of emotional stimuli, including facial expressions, non-verbal emotional sounds, or music [38]. This impairment is selective for negative emotions, and patients' ability for recognizing and reacting to positive emotions is often spared [39] or even disproportionately increased [40]. In addition to emotional recognition, patients with bvFTD have deficits in suppressing emotions, generating emotions, and perceiving self-conscious emotions [41]. Decreased grey matter volumes of the amygdala and AIC have been reported in bvFTD patients with impaired emotional recognition of facial expressions [42]. Amygdala atrophy, similar to AIC, occurs early in the course of bvFTD [43], and was consistently reported in our included studies. The amygdala has reciprocal connections to the ventral striatum, as well as limbic and paralimbic brain regions [43], and has a central role in recognition of emotions, but also in reward processing, motivation, attention, learning and memory [44]. In addition, the amygdala along with the temporal pole, ventral striatum, and thalamus, is responsible for the SN functions that include providing the AIC with the information about socio-emotional valence of the external and internal world. The information from these different sources is integrated in the AIC, where the salience of the current state is determined/represented, and passed on to more downstream regions [36].

Lack of empathy, i.e., impaired affective social cognition, is a core diagnostic feature of bvFTD [3] and is closely related to the deficits in emotional processing [45]. Empathy indicates an ability of identifying and sharing emotions and needs of other individuals [46]. Deficits in empathy can have a detrimental effect on the relationships of patients with their relatives and caregivers [47]. In addition, lack of empathy, and impaired social cognition in general, can result in disinhibition of socially inappropriate behaviors. More specifically, disinhibition might be a consequence of patients' inability to correctly identify social and emotional signals and their associated punishments/rewards, thereby neglecting the negative consequences of their own social acts [45]. Recent neuroimaging meta-analyses on healthy individuals have shown that empathy is consistently associated with activation of regions including the AIC, amygdala, ACC, thalamus, and lateral frontal regions [48, 49]. In addition, individual differences in socioemotional sensitivity has been shown to correlate with FC of the SN [50], and interestingly, socio-affective training aimed at improving empathy and compassion is associated with plasticity of the AIC [51]. Several neuroimaging studies on the neural correlates of empathy and social

cognition in bvFTD patients have pointed out to abnormalities in the similar regions, such as the insula, thalamus, amygdala, inferior frontal gyrus, lateral orbitofrontal cortex, and medial frontal regions including subcallosal and midcingulate cortex [40, 50, 52, 53]. Interestingly, similar regions are involved in impaired socio-emotional dysfunctions of other neuropsychiatric disorders such as autism spectrum disorder [54], conduct disorder [55], and schizophrenia [56].

Based on the 'simulation theory of empathy', humans use their own mind as a model to predict and understand the thoughts and feelings of others [34]. Therefore, and as self-awareness of affective states largely relies on interoception, i.e., awareness of internal bodily homeostatic state, it has been suggested that interoception has an important role in empathy [34, 57]. These two closely related functions are presumed to be mediated by the AIC, where dual and corresponding mappings for subjective and empathetic feeling states are represented [46]. In line with this hypothesis, a fMRI study demonstrated that when subjects are interoceptively aware (attending to their heartbeats), they show a higher empathy-related brain activity in the AIC after observing emotionally valent facial expressions [57]. Patients with bvFTD display impaired interoception, as has been shown by their decreased performance in the heartbeat detection task [58], or their lower sensitivity to pain and temperature [59], which interestingly is associated with the atrophy of insula and fronto-temporal regions [58]. The lack of empathy in bvFTD patients could therefore be partially attributable to the impairments in interoception, which are due to AIC dysfunction.

Based on our findings in the AIC, it is worthy to note that this convergent cluster was located more on the dorsal surface of the left AIC. This region, as suggested by previous studies and our functional decoding, is more involved in cognitive control and semantic functions [60], as opposed to the right and ventral AIC, which has a key role in socio-emotional processing [61]. Although we only include studies on bvFTD patients, this finding suggests that some studies might include bvFTD patients with concomitant language abnormalities or semantic variants of FTD. Nevertheless, the segregation of functions in the dorsal and ventral AIC is not as clear-cut and different functions of AIC have shown to converge on its dorsal surface [62]. In addition, our functional decoding analysis showed that the left dorsal AIC is more likely to be activated in interoception than in language functions, and as mentioned above, interoception is a key component of empathy. Of note, previous neuroimaging meta-analyses of empathy have also

shown activation of both left and right, as well as ventral and dorsal AIC in response to emotional stimuli [49].

4.2. Limbic system abnormalities in bvFTD result in executive dysfunction and apathy

The ACC, as the efferent hub of SN, coordinates initiation of appropriate behaviors in response to the states that are emotionally, socially, or homeostatically significant [36]. This function is mainly accomplished by switching the brain activity from the default mode network (DMN) to the central executive network (CEN), [63], which refers to the brain areas that are engaged during executive functions, i.e., cognitively demanding tasks that require sustained attention, including working memory, problem solving, planning, inhibiting, and development or implementation of strategies [64]. Executive dysfunction is a prominent symptom and a key diagnostic feature of bvFTD, which affects many domains of higher order brain functions, and contributes to development of apathy or inertia (see below) [65]. Meta-analytic studies have suggested that in healthy individuals, the frontoparietal and subcortical structures such as the dorsolateral prefrontal cortex, superior parietal lobules, dorsal ACC, thalamus, and striatum are involved in executive functions [64]. Accordingly, executive dysfunction in bvFTD patients is associated with atrophy of anterior cingulate and midcingulate gyri, medial frontal cortex, and lateral prefrontal cortex [66]. In the present meta-analysis, we found consistent abnormalities in the ACC and caudate nucleus in bvFTD patients. These regions were grouped together in the hierarchical clustering, and showed FC with each other, and other key regions of the CEN including the prefrontal cortex and superior parietal lobule. However, we found no consistent abnormality in the lateral frontal and parietal regions classically associated with executive functions. This finding suggests that in addition to the primary deficits in the ACC and striatum, executive dysfunction in bvFTD patients might be secondary to their inability to engage these lateral cortical regions due to dysfunction in the ACC and SN. Furthermore, as impairments in classical executive functioning tasks occur later in the course of bvFTD [67], some patients may not have yet developed abnormalities in lateral regions of the CEN, making it less likely to be identified consistently across the literature.

Psychopathology of apathy or inertia involves impairments in motivation, initiation and planning/execution [2]. Although all three components are dysfunctional in bvFTD patients, lack of motivation is the most prominent abnormality, which contributes to apathy [68]. Motivation

refers to the ability of associating positive or negative affective signals with the value of actions, and attempting to maximize value by seeking rewards and avoiding punishments [69]. In this context, abnormal reward processing can lead to a lack of motivation, both by reducing the inclination to perform and complete tasks and ability to comprehend the consequences of future actions [70]. Recent meta-analysis has shown that in healthy individuals, the striatum, insula, amygdala, thalamus, parahippocampal gyrus, and medial frontal regions such as the ACC are involved in reward processing [71]. We found convergent abnormalities in many of these reward-responsive regions including the left caudate, amygdala, paracingulate cortex, frontal medial cortex, and ACC. Interestingly, motivational deficits in bvFTD patients are associated with atrophy of the orbitofrontal cortex and ACC [72]. These findings suggest that lack of motivation in bvFTD patients occurs as a result of their decreased sensitivity to rewards and punishments, due to dysfunction of the ACC, orbitofrontal cortex, and striatum [70].

4.3. The role of medial temporal lobe atrophy in amnesic features of bvFTD

Classically, bvFTD has been mainly described as a predominantly behavioral disorder with less episodic memory impairment [3]. However, patients with bvFTD, like other dementia syndromes may have deficits in encoding and retrieval of autobiographical memories, comparable to that of AD [73]. It has been reported that impaired episodic memory functions in bvFTD patients is attributable to their executive dysfunction, i.e., their inability to properly monitor topics and events, check the relevance of incoming memories, and inhibit competing memories, due to frontal lobe abnormalities [33]. Although executive dysfunction can be a contributing factor to amnesia, it has been suggested that similar to AD, amnesic bvFTD patients have atrophy or dysfunction of the hippocampus and other medial temporal lobe (MTL) structures [73, 74]. Similarly, we found convergent atrophy in the CA1 and dentate gyrus of the right anterior hippocampus. This finding is rather new than previous neuroimaging meta-analyses on bvFTD, which reported no convergent abnormalities in the MTL [4, 8, 10]. These findings, however, suggest that MTL atrophy and impaired episodic memory exist in bvFTD, and therefore intact memory function may not constitute a suitable differentiating factor between bvFTD and AD [75]. An alternative explanation might be that as both bvFTD and AD are often diagnosed using clinical diagnostic criteria that are not certain [76, 77], a portion of clinically-diagnosed bvFTD patients, when assessed histopathologically, may actually have AD pathology (e.g., 12 out of 63

patients [76]), or that frontotemporal lobar degeneration (FTLD) and AD cover a spectrum of neurodegenerative disorders with some bvFTD patients also having underlying AD pathology (and vice versa) [78].

4.4. Potential strengths and limitations

We replicated some of the findings of previous meta-analyses on bvFTD in the frontomedial areas, AIC, and striatum, but in addition, we identified a cluster of convergence in the amygdala and hippocampus, probably by virtue of a higher number of structural and functional experiments and increased meta-analytic power. On the other hand, we found no convergence in some of the regions commonly reported in previous meta-analyses, namely lateral frontal cortical areas and thalamus. Of note, we used a stringent method of multiple comparison correction (i.e., cFWE). In addition, including both structural and functional experiments from various imaging modalities allowed us to identify regions that are both structurally and functionally impaired.

Our main limitation, which was in fact inherited from the included studies, was the heterogeneity of clinical samples, particularly with regard to the severity of symptoms, histopathological subtypes, and molecular etiology of bvFTD. Several studies have suggested that distinct pathological or genetic subtypes of frontotemporal lobar degeneration (FTLD) have different neuroanatomical correlates [79]. These subtypes are often difficult to determine, and therefore, very few studies had investigated them separately, preventing us from doing subgroup analyses on those specific subtypes. In addition, as most of the included studies had diagnosed bvFTD using the clinical criteria, it is possible that some of the patients had other disorders characterized by symptoms that can overlap with bvFTD, such as AD or other neuropsychiatric disorders [80]. Finally, a methodological limitation of our meta-analysis, which is common to all CBMA methods, was that the pooling of findings was based on the peak coordinates of significant regions. This method essentially ignores the volume and extent of clusters. Alternatively, image-based meta-analytic methods that are based on unthresholded statistical maps can overcome this issue, when enough number of experiments are available [81]. We also advocate for original neuroimaging studies to share their results as unthresholded statistical maps on open online platforms.

5. Conclusion

Using a large-scale ALE meta-analysis on both structural and functional brain studies of bvFTD and following the best-practice neuroimaging meta-analysis guidelines, we found consistent abnormalities in the AIC, paracingulate cortex and ACC, amygdala, hippocampus, and basal ganglia, across the literature. The MACM and RSFC maps revealed a significant overlap of task-based and task-free co-activation of the convergent clusters identified based on ALE meta-analysis with regions such as the striatum, thalamus, midline frontal regions, AIC, entorhinal cortex, posterior cingulate cortex, and cerebellum. Moreover, hierarchical analysis of the convergent clusters identified two functionally coherent sub-networks of the identified consistent regions, namely the insula-amygdala network and the cingulo-striatal network. Functional decoding of these regions using forward-inference demonstrated a significant contribution of these clusters processing of negative and positive emotions, interoception, reward processing, higher-order cognitive functions, as well as olfactory and gustatory perception. Overall, these findings suggest a central role of the SN and regions connected to it in the pathology of bvFTD, in line with previous models of bvFTD pathophysiology [36]. The AIC, as the afferent hub of the SN, is involved in detecting the emotional, homeostatic, social, and motivational salience of internal/external environment via inputs from regions such as amygdala. Thus, dysfunctions of the AIC and amygdala in bvFTD patients, can impair their socio-emotional processing, and may lead to disinhibition of socially inappropriate behaviors, and a lack of empathy. The midline frontal regions, and in particular pgACC, act as the efferent hub of the SN and in response to salient stimuli direct the brain resources towards a state where it can proportionally respond to these stimuli. In addition, these regions, along with the basal ganglia and amygdala, have a key role in reward processing. Hence, the abnormalities of midline frontal regions, basal ganglia, and amygdala in patients with bvFTD, may be responsible for their executive dysfunction, as well as apathy, primarily through a lack of motivation. In addition, we also observed convergent atrophy of anterior hippocampus in bvFTD patients, challenging the classical view that bvFTD is a predominantly behavioral disorder, sparing episodic memory, and suggesting that perhaps hippocampal atrophy and amnesic symptoms may not suitably differentiate bvFTD and AD. In general, our results highlighted a crucial role of the salience network and subcortical regions in pathophysiology of bvFTD.

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Figure 1. PRISMA flowchart of study selection. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Figure 2. Convergence of brain imaging findings in bvFTD compared to healthy controls across all experiments (A), experiments reporting atrophy/hypoactivation (B), and experiments using functional (C, orange) or structural (C, green) modalities. The coordinates are in MNI space. Color bars represent Z values. ALE: activation likelihood estimation, bvFTD: behavioral-variant frontotemporal dementia, MNI: Montreal Neurological Institute.

Figure 3. The overlap of resting-state functional connectivity and meta-analytic connectivity maps of convergent regions in the all-effects ALE. The coordinates are in MNI space. MACM: meta-analytic connectivity map, RSFC: resting-state functional connectivity, Amyg: amygdala, Hipp: hippocampus, Caud: caudate nucleus, SCC: subcallosal cortex, PrCC: paracingulate cortex, FMC: frontomedial cortex, AIC: anterior insular cortex, ACC: anterior cingulate cortex, ALE: activation likelihood estimation, MNI: Montreal Neurological Institute.

Figure 4. Hierarchical clustering of convergent regions in the all-effects ALE. Below the pair-wise functional connectivity matrix of the convergent regions is shown after Fischer's z-transformation and normalization to the maximum. Amyg: amygdala, Hipp: hippocampus, Caud: caudate nucleus, SCC: subcallosal cortex, PrCC: paracingulate cortex, FMC: frontomedial cortex, AIC: anterior insular cortex, ACC: anterior cingulate cortex, ALE: activation likelihood estimation.

Figure 5. Functional decoding analysis of convergent regions in the all-effects ALE based on BrainMap behavioral domain categories and subcategories. The spider plot values are likelihood ratios. Amyg: amygdala, Hipp: hippocampus, Caud: caudate nucleus, SCC: subcallosal cortex, PrCC: paracingulate cortex, FMC: frontomedial cortex, AIC: anterior insular cortex, ACC: anterior cingulate cortex, ALE: activation likelihood estimation.

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Supplementary Figure 1. Meta-analytic connectivity mapping of convergent regions in the all-effects activation likelihood estimation. The coordinates are in MNI space. Amyg: amygdala, Hipp: hippocampus, Caud: caudate nucleus, SCC: subcallosal cortex, PrCC: paracingulate cortex, FMC: frontomedial cortex, AIC: anterior insular cortex, ACC: anterior cingulate cortex.

Supplementary Figure 2. Resting-state functional connectivity maps of convergent regions in the all-effects activation likelihood estimation. The coordinates are in MNI space. Amyg: amygdala, Hipp: hippocampus, Caud: caudate nucleus, SCC: subcallosal cortex, PrCC: paracingulate cortex, FMC: frontomedial cortex, AIC: anterior insular cortex, ACC: anterior cingulate cortex.

Supplementary Table 1. Final studies included in the meta-analysis. (bvFTD: Behavioral variant of Frontotemporal dementia, MNI: Montreal Neurological Institute atlas , VBM: Voxel-based morphometry, PET: 18F-fluorodeoxyglucose positron emission tomography, rs-fMRI: Resting-state functional magnetic resonance imaging, t-fMRI: Task-based functional magnetic resonance imaging, N/A: The required information was not available)

Ref.	Study	Control			bvFTD			Space	Imaging Method
		Numbers	Mean Age	Mean Years of Education	Numbers	Mean Age	Mean Years of Education		
[1]	Lee et al. 2014	42	62.2	15.9	C9orf72 carriers: 14 Non-carrier: 14	C9orf72 carriers: 58.3 Non-carrier: 60.8	C9orf72 carriers: 14.9 Non-carrier: 16.4	MNI	VBM
[2]	Seeley et al. 2008	45	68.3	16.4	15	65.9	14.7	MNI	VBM
[3]	Mandelli et al. 2016	25	62.3	16.4	13	62.9	16.1	MNI	VBM
[4]	Agosta et al. 2009	56	66.57	16.58	31	58.53	15.95	MNI	VBM
[5]	Chiong et al. 2013	48	66	17.7	8	61.2	16.6	MNI	VBM
[6]	Lagarde et al. 2013	18	67.8	11.55	16	69.25	11.75	MNI	VBM
[7]	Lagarde et al. 2016	18	67.8	11.6	18	69.7	12	MNI	VBM
[8]	Kumfor et al. 2018	20	66.3	14.2	19	62.7	12.6	MNI	VBM
[9]	Kamminga et al. 2015	14	65.8	11.2	13	60.5	11.3	MNI	VBM
[10]	Kumfor et al. 2014	10	71.3	14.9	13	66.5	11.1	MNI	VBM
[11]	Kumfor et al. 2015	10	68.6	14.8	10	62.5	12	MNI	VBM
[12]	Kumfor et al. 2018 (a)	28	63.9	12.5	55	62.9	11.8	MNI	VBM
[13]	Kumfor et al. 2017	21	64.8	13.7	22	65	11.1	MNI	VBM
[14]	Hutchings et al. 2015	14	70.78	13.7	13	64.05	11.8	MNI	VBM
[15]	Kumfor et al. 2013	27	64.3	13.6	18	63.8	11.9	MNI	VBM
[16]	Ahmed et al. 2016	25	66	13.8	19	62	11.9	MNI	VBM
[17]	Devenney et al. 2015	25	N/A	13.4	Probable bvFTD: 38 Possible bvFTD: 20	N/A	Probable bvFTD: 12.5 Possible bvFTD: 10.8	MNI	VBM
[18]	Ahmed et al. 2019	19	62.9	N/A	26	60.9	N/A	MNI	VBM
[19]	Donnelly-kehoe et al. 2019	60	63.91	14.83	44	66.72	13.75	MNI	VBM
[20]	Kumfor et al.	20	65.2	13.8	16	60.7	11.2	MNI	VBM

	2018 (b)								
[21]	Wei et al. 2019	26	64.69	14.47	36	61.05	11.92	MNI	VBM
[22]	Wilson et al. 2019	22	66.1	14.2	18	62.5	11.8	MNI	VBM
[23]	Irish et al. 2013 (a)	10	69.2	12.7	10	62.8	11.8	MNI	VBM
[24]	Irish et al. 2013 (b)	19	68.1	13.1	19	63.6	12.6	MNI	VBM
[25]	Irish et al. 2014 (a)	14	72.2	11.9	11	62.4	11.9	MNI	VBM
[26]	Irish et al. 2016	20	67.1	13.3	15	63.5	11.6	MNI	VBM
[27]	Dermody et al. 2016	12	69	13.6	12	63.2	11.6	MNI	VBM
[28]	Dermody et al. 2015	22	68.2	14	24	63	12.4	MNI	VBM
[29]	Hornberger et al. 2011	18	64.8	13.6	14	59.3	11.8	MNI	VBM
[30]	Chen et al. 2018 (a)	35	64.4	13.4	45	60.9	11.6	MNI	VBM
[31]	Irish et al. 2014 (b)	14	68	13.7	10	63.6	10.9	MNI	VBM
[32]	O'Callaghan et al. 2019	24	66.3	N/A	35	61.4	N/A	MNI	VBM
[33]	Tu et al. 2015	23	68	13.3	24	64.7	11.8	MNI	VBM
[34]	Baez et al. 2017	22	62.5	14.2	16	65.8	14.8	MNI	VBM
[35]	Baez et al. 2016 (a)	23	62.69	15.65	26	66.08	15.24	MNI	VBM
[36]	Baez et al. 2016 (b)	19	60.42	15.21	21	63.8	14.23	MNI	VBM
[37]	Cousins et al. 2016	18	68.6	15.6	18	63.9	16.3	MNI	VBM
[38]	McMillan et al. 2013	16	64.4	14.3	16	64.3	15.4	MNI	VBM
[39]	Grossman et al. 2004	25	N/A	N/A	14	63.07	15.07	MNI	VBM
[40]	Morgan et al. 2011	40	65.9	15	8	64.9	14.6	MNI	VBM
[41]	Libon et al. 2009	16	N/A	N/A	51	61.31	15.58	MNI	VBM
[42]	Nevler et al. 2017	17	66	16.3	32	63	15.7	MNI	VBM
[43]	Massimo et al. 2012	30	N/A	N/A	37	63.69	15.57	Talairach	VBM
[44]	Ash et al. 2016	27	67.1	14.9	32	63.7	15.7	MNI	VBM
[45]	Healy et al. 2015	35	70.2	15.54	9	65.3	15.75	MNI	VBM
[46]	Kanda et al. 2008	29	65.2	N/A	13	64.9	N/A	MNI	VBM, PET
[47]	Franceschi et al. 2005	24	N/A	N/A	6	61	12	MNI	PET
[48]	Salmon et al.	58	60.1	N/A	29	61.5	N/A	MNI	PET

	2003								
[49]	Tuovinen et al. 2017	25	59.6	N/A	21	60.7	N/A	MNI	VBM, rs-fMRI
[50]	Rytty et al. 2013	19	57.8	N/A	19	60.3	N/A	MNI	VBM, rs-fMRI
[51]	Melloni et al. 2016	22	68.31	13.06	26	67.96	13.92	MNI	VBM
[52]	Fernandez-Matarrubia et al. 2017	24	67.4	9.3	Amnesic-FTD: 26 Non-Amnesic-FTD: 13	Amnesic-FTD: 71.3 Non-Amnesic-FTD: 71.6	Amnesic-FTD: 8 Non-Amnesic-FTD: 6.8	MNI	PET
[53]	Matias et al. 2018	19	64.89	13.89	19	71.05	8.21	MNI	PET
[54]	Hafkemeijer et al. 2016	22	63.8	5.6	12	64.7	5	MNI	VBM
[55]	Farb et al. 2013	16	67.2	16.2	8	66.7	16	MNI	VBM
[56]	Bertoux et al. 2018	20	71.72	12.86	12	67.17	12.14	MNI	VBM
[57]	Santmaria-Garcia et al. 2016	30	60.1	13.22	16	57	14.67	MNI	VBM
[58]	Boccardi et al. 2005	26	69	8	9	62	6	MNI	VBM
[17]	Devenocchio et al. 2018	VBM: 20 PET: 48	VBM: 49.8 PET: 68.3	VBM: 14.3 PET: 10.3	VBM: 21 PET: 23	VBM: 72.1 PET: 71	VBM: 10.8 PET: 10.6	MNI	VBM, PET
[59]	Jeong et al. 2005	11	61.9	N/A	29	59.2	N/A	MNI	PET
[60]	Diehl et al. 2004	15	61.8	N/A	25	62.2	N/A	Talairach	PET
[61]	Laws et al. 2007	16	64.89	N/A	H1 Homozygotes: 31 H2 Carriers: 10	H1 Homozygotes: 62.4 H2 Carriers: 62.7	H1 Homozygotes: N/A H2 Carriers: N/A	Talairach	PET
[62]	Perneckzy et al. 2007	16	67.88	12.78	29	62.34	12.31	Talairach	PET
[63]	Grimmer et al. 2004	15	61.8	N/A	10	59.9	N/A	Talairach	PET
[64]	Peters et al. 2006	23	64	N/A	23	63.5	N/A	MNI	PET
[65]	Raczka et al. 2010	9	59.3	N/A	7	60	N/A	MNI	PET
[66]	Sheelakumari et al. 2019	20	62.8	15.63	25	63.68	17.03	MNI	VBM
[67]	Caminiti et al. 2015	30	58.84	13.56	12	63.11	12.08	MNI	rs-fMRI
[68]	Verfaillie et al. 2015	10	56	N/A	12	61	N/A	MNI	PET
[69]	Meyer et al. 2017	First group: 19	First group: 63.1	First group: N/A	First group: 19 Second group:	First group: 61.5 Second group:	First group: N/A Second group:	MNI	VBM

		Second group: 52	Second group: 63.1	Second group: N/A	52	61.5	N/A		
[70]	Garcia-Cordero et al. 2015	14	57.21	16.14	11	64.81	14.45	MNI	VBM
[71]	Kipps et al. 2009	16	66.4	N/A	11	62.1	N/A	MNI	VBM
[72]	Morbelli et al. 2016	20	64.4	13.4	25	60.9	11.6	Talairach	VBM, PET
[73]	Augustus et al. 2015	11	64	N/A	15	64	N/A	MNI	t-fMRI

Supplementary Table 2. The excluded studies and the reason for their exclusion. (Not bv: The imaging analysis was not performed on the behavioral variant of frontotemporal dementia patients/other types of demented patients were included, Data Not Reported: The coordinates that were needed to perform the meta-analysis were not provided in the article or by the corresponding author when contacted, ROI: The study was excluded for performing analysis on region(s) of interest or a seed was used in functional connectivity studies, Not Case Control: The between-group contrasts was not performed between healthy controls and behavioral variant frontotemporal dementia patients)

Title of The Article	Reason for Exclusion
(18)F-florataucipir (AV-1451) tau PET in frontotemporal dementia syndromes	18F-florataucipir and 11C-PiB PET Imaging
[(18)F]-AV-1451 tau PET imaging in Alzheimer's disease and suspected non-AD tauopathies using a late acquisition time window	[18F]-AV-1451 tau PET Imaging
[18F]FDG-PET in a case of right temporal lobe variant of frontotemporal dementia	Case Report
11C-DTBZ and 18F-FDG PET measures in differentiating dementias.	Not bv
18F-florbetapir PET in patients with frontotemporal dementia and Alzheimer disease.	18F-florbetapir PET Imaging
A Case of Crossed Logopenic Primary Progressive Aphasia in a Dextral Patient with Underlying Frontotemporal Dementia	Case Report
A critical role for the hippocampus in the valuation of imagined outcomes.	Data Not Reported
A multivariate metabolic imaging marker for behavioral variant frontotemporal dementia	Data Not Reported
A neural network underlying intentional emotional facial expression in neurodegenerative disease.	Data Not Reported
A non-DM1, non-DM2 multisystem myotonic disorder with frontotemporal dementia: phenotype and suggestive mapping of the DM3 locus to chromosome 15q21-24.	Not bv
A physiological signature of sound meaning in dementia.	ROI
A tensor based morphometry study of longitudinal gray matter contraction in FTD.	Tensor Based Morphometry
A visual MRI atrophy rating scale for the amyotrophic lateral sclerosis-frontotemporal dementia continuum.	ROI
A volumetric magnetic resonance imaging study of the amygdala in frontotemporal lobar degeneration and Alzheimer's disease.	ROI
Active lifestyles moderate clinical outcomes in autosomal dominant frontotemporal degeneration	Not bv
Affective mentalizing and brain activity at rest in the behavioral variant of frontotemporal dementia.	ROI
Agreement among neuropsychological and behavioral data and PiB findings in diagnosing Frontotemporal Dementia.	Not bv
Alterations of the sense of "humanness" in right hemisphere predominant frontotemporal dementia patients.	Irrelevant
Altered functional connectivity in asymptomatic MAPT subjects: a comparison to bvFTD.	ROI
Altered speech-related cortical network in frontotemporal dementia	ROI
Alzheimer Disease and Behavioral Variant Frontotemporal Dementia: Automatic Classification Based on Cortical Atrophy for Single-Subject Diagnosis.	Irrelevant
Alzheimer's disease and frontotemporal dementia exhibit distinct atrophy-behavior correlates: a computer-assisted imaging study.	Not bv
Amygdala subnuclei are differentially affected in the different genetic and pathological forms of frontotemporal dementia	ROI
Amygdaloid atrophy in frontotemporal dementia and Alzheimer's disease.	ROI
Amyloid imaging with (18)F-florbetaben in Alzheimer disease and other dementias.	ROI
Amyloid Imaging With 11C-PIB in Patients With Cognitive Impairment in a Clinical Setting: A Visual and Semiquantitative Analysis.	11C-PiB PET Imaging
Amyloid in dementia associated with familial FTLT: not an innocent bystander.	Not Case Control

An advanced white matter tract analysis in frontotemporal dementia and early-onset Alzheimer's disease.	Diffusion-weighted imaging
An investigation of care-based vs. rule-based morality in frontotemporal dementia, Alzheimer's disease, and healthy controls.	Cortical Thickness
Analyzing theory of mind impairment in patients with behavioral variant frontotemporal dementia	No Voxel-Based Morphometry Was Performed on MRI Images.
Anatomic correlates of stereotypies in frontotemporal lobar degeneration.	Data Not Reported
Anatomical correlates of non-verbal perception in dementia patients	Data Not Reported
Anatomical correlates of reward-seeking behaviours in behavioural variant frontotemporal dementia.	Not Case Control
Anosognosia for behavioral disturbances in frontotemporal dementia and corticobasal syndrome: A voxel-based morphometry study.	Not Case Control
Antemortem differential diagnosis of dementia pathology using structural MRI: Differential-STAND.	No Voxel-Based Morphometry Was Performed on MRI Images.
Anterior brain glucose hypometabolism predates dementia in progranulin mutation carriers.	Not bv
Anti-Cholinergic Derangement of Cortical Metabolism on 18F-FDG PET in a Patient with Frontotemporal Lobar Degeneration Dementia: A Case of the TREDEM Registry	Case Report
Apathy and disinhibition in frontotemporal dementia: Insights into their neural correlates.	Data Not Reported
Apathy and impulsivity in frontotemporal lobar degeneration syndromes.	Data Not Reported
Apathy in frontotemporal dementia: behavioral and neuroimaging correlates.	Data Not Reported
Apathy is not associated with basal ganglia atrophy in frontotemporal dementia.	Not bv
APOE and modulation of Alzheimer's and frontotemporal dementia.	Not bv
Applying Automated MR-Based Diagnostic Methods to the Memory Clinic: A Prospective Study.	Irrelevant
Arterial spin labeling-based Z-maps have high specificity and positive predictive value for neurodegenerative dementia compared to FDG-PET.	Data Not Reported
Assessment of Eating Behavior Disturbance and Associated Neural Networks in Frontotemporal Dementia.	Data Not Reported
Assessment of executive function declines in presymptomatic and mildly symptomatic familial frontotemporal dementia: NIH-EXAMINER as a potential clinical trial endpoint	Not bv
Assessment of mild dementia with amyloid and dopamine terminal positron emission tomography.	Not bv
Assessment of Patient Self-awareness and Related Neural Correlates in Frontotemporal Dementia and Corticobasal Syndrome.	Not Case Control
Association Between Social Cognition Changes and Resting State Functional Connectivity in Frontotemporal Dementia, Alzheimer's Disease, Parkinson's Disease, and Healthy Controls	Number of Patients Below 6 bv
Association between the extended tau haplotype and frontotemporal dementia.	Not bv
Association of Cognitive and Behavioral Features Between Adults With Tuberous Sclerosis and Frontotemporal Dementia	Not bv
Association of the tau haplotype H2 with age at onset and functional alterations of glucose utilization in frontotemporal dementia.	Data Not Reported
Association of the TBK1 mutation p.Ile334Thr with frontotemporal dementia and literature review	Review Article
Atrophy in two attention networks is associated with performance on a Flanker task in neurodegenerative disease.	Data Not Reported
Atrophy measurement of the anterior commissure and substantia innominata with 3T high-resolution MR imaging: does the measurement differ for patients with frontotemporal lobar degeneration and Alzheimer disease and for healthy subjects?	Not bv
Atrophy patterns in histologic vs clinical groupings of frontotemporal lobar degeneration	Number of Patients Below 6
Atrophy rates of the cingulate gyrus and hippocampus in AD and FTL D.	Not bv
Atypical presentation of a novel Presenilin 1 R377W mutation: sporadic, late-onset Alzheimer disease with epilepsy and frontotemporal atrophy.	Case Report
Atypical, slowly progressive behavioural variant frontotemporal dementia associated with C9ORF72	Case Report

hexanucleotide expansion.	
Auditory conflict and congruence in frontotemporal dementia.	Data Not Reported
Auditory hedonic phenotypes in dementia: A behavioural and neuroanatomical analysis.	Not bv
Autobiographical memory and patterns of brain atrophy in frontotemporal lobar degeneration.	Not bv
Automatic classification of MR scans in Alzheimer's disease.	Irrelevant
B-spline-based stereotactical normalization of brain FDG PET scans in suspected neurodegenerative disease: impact on voxel-based statistical single-subject analysis.	Not bv
Based on the Network Degeneration Hypothesis: Separating Individual Patients with Different Neurodegenerative Syndromes in a Preliminary Hybrid PET/MR Study.	Data Not Reported
Behavioral disorders in the frontal and temporal variants of frontotemporal dementia.	No Voxel-Based Morphometry Was Performed on MRI Images.
Behavioral variant frontotemporal dementia with corticobasal degeneration pathology: phenotypic comparison to bvFTD with Pick's disease.	Irrelevant
Behavioral variant of frontotemporal dementia or frontal variant of Alzheimer's disease? A case study	Case Report
Behavioral-variant frontotemporal dementia: Distinct phenotypes with unique functional profiles.	Data Not Reported
Behavioural variant frontotemporal dementia: At the interface of interoception, emotion and social cognition?	Commentary
Binge eating is associated with right orbitofrontal-insular-striatal atrophy in frontotemporal dementia.	Not bv
Brain and ventricular volumetric changes in frontotemporal lobar degeneration over 1 year.	Not Case Control
Brain atrophy over time in genetic and sporadic frontotemporal dementia: a study of 198 serial magnetic resonance images.	Not bv
Brain Connectivity and Information-Flow Breakdown Revealed by a Minimum Spanning Tree-Based Analysis of MRI Data in Behavioral Variant Frontotemporal Dementia	Connectivity Matrices (Minimum Spanning Tree-Based Analysis of MRI Data)
Brain magnetic resonance imaging structural changes in a pedigree of asymptomatic progranulin mutation carriers.	Not bv
Brain network connectivity assessed using graph theory in frontotemporal dementia.	ROI
Brain network connectivity differs in early-onset neurodegenerative dementia.	Data Not Reported
Brain Network Organization and Social Executive Performance in Frontotemporal Dementia.	ROI
Building a new paradigm for the early recognition of behavioral variant frontotemporal dementia: Late Onset Frontal Lobe Syndrome study.	Not Case Control
Carbon-11-Pittsburgh compound B positron emission tomography imaging of amyloid deposition in presenilin 1 mutation carriers.	Irrelevant
Case report of first-episode psychotic symptoms in a patient with early-onset Alzheimer's disease	Case Report
Caudate nucleus volumes in frontotemporal lobar degeneration: differential atrophy in subtypes.	ROI
Cerebellar integrity in the amyotrophic lateral sclerosis-frontotemporal dementia continuum.	ROI
Cerebral hypometabolism and grey matter density in MAPT intron 10 +3 mutation carriers.	Not Case Control
Cerebral perfusion changes in presymptomatic genetic frontotemporal dementia: a GENFI study	Not bv
Cerebral white matter degeneration in frontotemporal dementia detected by diffusion-weighted magnetic resonance imaging.	DWI
Characteristics of frontotemporal dementia patients with a Progranulin mutation.	Not bv
Characterizing radiology reports in patients with frontotemporal dementia.	Irrelevant
Cholinergic imaging in corticobasal syndrome, progressive supranuclear palsy and frontotemporal dementia.	Data Not Reported
Citalopram Improves Obsessive-Compulsive Crossword Puzzling in Frontotemporal Dementia	Case Report
Clinical and neuroanatomical signatures of tissue pathology in frontotemporal lobar degeneration.	Not bv
Clinical and neuroimaging investigations of language disturbance in frontotemporal dementia-motor	Not bv

neuron disease patients	
Clinical characteristics of frontotemporal patients with symmetric brain atrophy.	ROI
Clinical characteristics of patients with frontotemporal dementia with and without lobar atrophy on MRI.	No Voxel-Based Morphometry Was Performed on MRI Images.
Clinical features of TBK1 carriers compared with C9orf72, GRN and non-mutation carriers in a Belgian cohort.	Irrelevant
Clinical Utility of Amyloid PET Imaging in the Differential Diagnosis of Atypical Dementias and Its Impact on Caregivers.	Irrelevant
Clinicopathological and imaging correlates of progressive aphasia and apraxia of speech.	Irrelevant
Clinicopathological correlations in behavioural variant frontotemporal dementia.	Not Case Control
Cognitive reserve and TMEM106B genotype modulate brain damage in presymptomatic frontotemporal dementia: a GENFI study.	Not bv
Cognitive reserve in frontotemporal degeneration Neuroanatomic and neuropsychological evidence	Not bv
Cognitive reserve in granulin-related frontotemporal dementia: from preclinical to clinical stages.	Not bv
Combined evaluation of FDG-PET and MRI improves detection and differentiation of dementia.	Not bv
Combined magnetic resonance imaging and positron emission tomography brain imaging in behavioural variant frontotemporal degeneration: refining the clinical phenotype.	No Case Control
Comparison of Gray Matter Atrophy in Behavioral Variant Frontal Temporal Dementia and Amyotrophic Lateral Sclerosis: A Coordinate-Based Meta-Analysis	Meta-Analysis
Comparison of impaired subcortico-frontal metabolic networks in normal aging, subcortico-frontal dementia, and cortical frontal dementia.	Data Not Reported
Comparison of Prefrontal Atrophy and Episodic Memory Performance in Dysexecutive Alzheimer's Disease and Behavioral-Variant Frontotemporal Dementia.	ROI
COMT Val158Met genotype influences neurodegeneration within dopamine-innervated brain structures.	Data Not Reported
Concordance and discordance between brain perfusion and atrophy in frontotemporal dementia.	Not bv
Concurrent white and gray matter degeneration of disease-specific networks in early-stage Alzheimer's disease and behavioral variant frontotemporal dementia.	ROI
Confirmation of (123)I-FP-CIT-SPECT (ioflupane) quantification methods in dementia with Lewy body and other neurodegenerative disorders	ROI
Conflict monitoring in early frontotemporal dementia.	Cortical Volumes calculated by FreeSurfer
Contrasting metabolic impairment in frontotemporal degeneration and early onset Alzheimer's disease.	Not bv
Contrasting prefrontal cortex contributions to episodic memory dysfunction in behavioural variant frontotemporal dementia and Alzheimer's disease.	Data Not Reported
Contribution of CSF biomarkers to early-onset Alzheimer's disease and frontotemporal dementia neuroimaging signatures	Cortical thickness and fraction anisotropy (FA) maps calculated by FreeSurfer and FSL
Correlation of ventricular asymmetry with metabolic asymmetry in frontotemporal dementia.	Not bv
Correlations between clinical characteristics and neuroimaging in Chinese patients with subtypes of frontotemporal lobe degeneration.	Not Case Control
Corrigendum: Behavioral and Neuroimaging Evidence for Facial Emotion Recognition in Elderly Korean Adults with Mild Cognitive Impairment, Alzheimer's Disease, and Frontotemporal Dementia	Not bv
Cortical microstructure in the behavioural variant of frontotemporal dementia: looking beyond atrophy	Cortical thickness and cortical mean diffusivity were computed using a surface-based approach
Cortical morphometric subclassification of frontotemporal lobar degeneration.	ROI
Cortical Thickness and Surface Area Networks in Healthy Aging, Alzheimer's Disease and Behavioral Variant Fronto-Temporal Dementia	No voxel-Based Morphometry Was Performed on MRI Images.
Cortical volumes and atrophy rates in FTD-3 CHMP2B mutation carriers and related non-carriers.	Irrelevant

Damage to left frontal regulatory circuits produces greater positive emotional reactivity in frontotemporal dementia.	Data Not Reported
Data-driven regions of interest for longitudinal change in frontotemporal lobar degeneration.	ROI
Data-driven regions of interest for longitudinal change in three variants of frontotemporal lobar degeneration.	ROI
Decline of cerebral glucose metabolism in frontotemporal dementia: a longitudinal 18F-FDG-PET-study.	Data Not Reported
Decomposition of metabolic brain clusters in the frontal variant of frontotemporal dementia.	Irrelevant
Deconstructing empathy: Neuroanatomical dissociations between affect sharing and prosocial motivation using a patient lesion model.	Data Not Reported
Deep clinical and neuropathological phenotyping of Pick disease.	Using staining and immunohistochemistry methods
Deformation-based morphometry reveals brain atrophy in frontotemporal dementia.	Not bv
Degradation of cognitive timing mechanisms in behavioural variant frontotemporal dementia.	Data Not Reported
Dementia induces correlated reductions in white matter integrity and cortical thickness: a multivariate neuroimaging study with sparse canonical correlation analysis.	DWI
Depressive symptoms and white matter changes in patients with dementia.	Not bv
Detailed volumetric analysis of the hypothalamus in behavioral variant frontotemporal dementia.	ROI
Detecting sarcasm from paralinguistic cues: anatomic and cognitive correlates in neurodegenerative disease.	Data Not Reported
Development of an MRI rating scale for multiple brain regions: comparison with volumetrics and with voxel-based morphometry.	ROI
Diagnostic Accuracy of MRI and Additional [18F]FDG-PET for Behavioral Variant Frontotemporal Dementia in Patients with Late Onset Behavioral Changes.	Irrelevant
Diagnostic classification of arterial spin labeling and structural MRI in presenile early stage dementia.	Arterial spin labeling
Diagnostic imaging of dementia with Lewy bodies, frontotemporal lobar degeneration, and normal pressure hydrocephalus	Review Article
Diagnostic patterns of regional atrophy on MRI and regional cerebral blood flow change on SPECT in young onset patients with Alzheimer's disease, frontotemporal dementia and vascular dementia.	99mTc-HMPAO SPECT
Diagnostic utility of ASL-MRI and FDG-PET in the behavioral variant of FTD and AD	Data Not Reported
Diagnostic Value of Diffusion Tensor Imaging and Positron Emission Tomography in Early Stages of Frontotemporal Dementia.	DWI
Diagnostic value of high signal abnormalities on T2 weighted MRI in the differentiation of Alzheimer's, frontotemporal and vascular dementias.	No Voxel-Based Morphometry Was Performed on MRI Images.
Differences in gray and white matter (18)F-THK5351 uptake between behavioral-variant frontotemporal dementia and other dementias	ROI
Differences in structural covariance brain networks between behavioral variant frontotemporal dementia and Alzheimer's disease.	Data Not Reported
Different FDG-PET metabolic patterns at single-subject level in the behavioral variant of frontotemporal dementia.	Not Case Control
Different patterns of cortical gray matter loss over time in behavioral variant frontotemporal dementia and Alzheimer's disease.	Cortical thickness calculation by surface construction and DWI
Different regional patterns of cortical thinning in Alzheimer's disease and frontotemporal dementia.	Cortical thickness calculation by surface construction
Differential diagnosis of neurodegenerative diseases using structural MRI data.	Irrelevant
Differential effects of global and cerebellar normalization on detection and differentiation of dementia in FDG-PET studies.	ROI
Differential insular cortex sub-regional atrophy in neurodegenerative diseases: a systematic review and meta-analysis	Systematic Review and Meta-Analysis
Differential putaminal morphology in Huntington's disease, frontotemporal dementia and Alzheimer's disease.	ROI

Differential topography of Alzheimer's disease and frontotemporal dementia: an MRI volumetric analysis from Sunnybrook dementia study.	paper and abstract not available
Differentiating primary progressive aphasia in a brief sample of connected speech.	Irrelevant
Diffusion tensor tractography versus volumetric imaging in the diagnosis of behavioral variant frontotemporal dementia.	ROI
Direct prospective comparison of (18)F-FDG PET and arterial spin labelling MR using simultaneous PET/MR in patients referred for diagnosis of dementia	Number of Patients Below 6
Discrete Neural Correlates for the Recognition of Negative Emotions: Insights from Frontotemporal Dementia.	Data Not Reported
Discriminant validity and neuroanatomical correlates of rule monitoring in frontotemporal dementia and Alzheimer's disease.	ROI
Disease state fingerprint in frontotemporal degeneration with reference to Alzheimer's disease and mild cognitive impairment.	Irrelevant
Disease-specific patterns of cortical and subcortical degeneration in a longitudinal study of Alzheimer's disease and behavioural-variant frontotemporal dementia.	Cortical thickness calculation by surface construction
Disentangling Heterogeneity in Alzheimer's Disease and Related Dementias Using Data-Driven Methods	Review Article
Disrupted rich club network in behavioral variant frontotemporal dementia and early-onset Alzheimer's disease.	DWI
Dissociating behavioral disorders in early dementia-An FDG-PET study.	Number of Patients Below 6
Dissociating memory networks in early Alzheimer's disease and frontotemporal lobar degeneration - a combined study of hypometabolism and atrophy.	Number of Patients Below 6
Dissociation of Structural and Functional Integrities of the Motor System in Amyotrophic Lateral Sclerosis and Behavioral-Variant Frontotemporal Dementia.	ROI
Distinct anatomical subtypes of the behavioural variant of frontotemporal dementia: a cluster analysis study.	ROI
Distinct antemortem profiles in patients with pathologically defined frontotemporal dementia.	Not bv
Distinct MRI atrophy patterns in autopsy-proven Alzheimer's disease and frontotemporal lobar degeneration.	Not bv
Distinct neuroanatomical substrates and cognitive mechanisms of figure copy performance in Alzheimer's disease and behavioral variant frontotemporal dementia.	Cortical thickness calculation by surface construction
Distinct profiles of brain atrophy in frontotemporal lobar degeneration caused by progranulin and tau mutations.	Not bv
Distinct Subtypes of Behavioral Variant Frontotemporal Dementia Based on Patterns of Network Degeneration.	ROI
Divergent network connectivity changes in behavioural variant frontotemporal dementia and Alzheimer's disease.	ROI
Does TDP-43 type confer a distinct pattern of atrophy in frontotemporal lobar degeneration?	Not bv
Dominant hemisphere lateralization of cortical parasympathetic control as revealed by frontotemporal dementia.	ROI
Dual-phase [18F]florbetapir in frontotemporal dementia	[18F]florbetapir PET scan
Dyslexia susceptibility genes influence brain atrophy in frontotemporal dementia.	Not Case Control
Early 11C-PIB frames and 18F-FDG PET measures are comparable: a study validated in a cohort of AD and FTL D patients.	ROI
Early-stage differentiation between presenile Alzheimer's disease and frontotemporal dementia using arterial spin labeling MRI.	Arterial spin labeling MRI
Eating and hypothalamus changes in behavioral-variant frontotemporal dementia.	ROI
Eating behavior in frontotemporal dementia: Peripheral hormones vs hypothalamic pathology.	ROI
Education modulates brain maintenance in presymptomatic frontotemporal dementia	Not bv
Energy expenditure in frontotemporal dementia: a behavioural and imaging study.	ROI

Enhanced positive emotional reactivity undermines empathy in behavioral variant frontotemporal dementia	Data Not Reported
Episodic memory and regional atrophy in frontotemporal lobar degeneration.	Not bv
Executive Abilities as Reflected by Clock Hand Placement: Frontotemporal Dementia Versus Early-Onset Alzheimer Disease.	Tensor Based Morphometry
Executive and behavioral deficits share common neural substrates in frontotemporal lobar degeneration - a pilot FDG-PET study.	Not bv
Executive deficits are related to the inferior frontal junction in early dementia.	Not Case Control
Executive dysfunction in frontotemporal dementia and corticobasal syndrome.	Data Not Reported
Exploring quantitative group-wise differentiation of Alzheimer's disease and behavioural variant frontotemporal dementia using tract-specific microstructural white matter and functional connectivity measures at multiple time points	ROI
Extrapyramidal symptoms in Frontotemporal Dementia: prevalence and clinical correlations.	Not bv
Face shape and face identity processing in behavioral variant fronto-temporal dementia: A specific deficit for familiarity and name recognition of famous faces.	Data Not Reported
Fair play: social norm compliance failures in behavioural variant frontotemporal dementia.	ROI
False Recognition in Behavioral Variant Frontotemporal Dementia and Alzheimer's Disease-Disinhibition or Amnesia?	ROI
FDG-PET improves accuracy in distinguishing frontotemporal dementia and Alzheimer's disease.	Not bv
Fear conditioning in frontotemporal lobar degeneration and Alzheimer's disease.	Not bv
First symptoms--frontotemporal dementia versus Alzheimer's disease.	Not Case Control
Flavour identification in frontotemporal lobar degeneration.	Data Not Reported
Fluorodeoxyglucose positron emission tomography in semantic dementia after 6 months of memantine: an open-label pilot study.	Irrelevant
Fluorodeoxyglucose-positron emission tomography in the differential diagnosis of early-onset dementia: a prospective, community-based study.	Irrelevant
Frequency of ubiquitin and FUS-positive, TDP-43-negative frontotemporal lobar degeneration.	Not bv
Frontal asymmetry in behavioral variant frontotemporal dementia: clinicoimaging and pathogenetic correlates.	Data Not Reported
Frontal network syndrome testing: clinical tests and positron emission tomography brain imaging help distinguish the 3 most common dementia subtypes.	Not Case Control
Frontal variant of Alzheimer's disease with asymmetric presentation mimicking frontotemporal dementia: Case report and literature review	Case Report
Fronto-striatal atrophy correlates of inhibitory dysfunction in Parkinson's disease versus behavioural variant frontotemporal dementia.	ROI
Frontotemporal asymmetry in socioemotional behavior: A pilot study in frontotemporal dementia	Cortical Volumes calculated by FreeSurfer
Frontotemporal brain sagging syndrome: an SIH-like presentation mimicking FTD.	Irrelevant
Frontotemporal dementia and its variants: What to look for	Under 6 No. of Patients
Frontotemporal dementia and language networks: cortical thickness reduction is driven by dyslexia susceptibility genes.	Not Case Control
Frontotemporal dementia associated with the C9ORF72 mutation: a unique clinical profile.	Not bv
Frontotemporal dementia can be distinguished from Alzheimer's disease and subcortical white matter dementia by an anterior-to-posterior rCBF-SPET ratio.	Single-photon emission tomography (SPET; (99m)Tc-HMPAO)
Frontotemporal dementia due to C9ORF72 mutations: clinical and imaging features.	Not Case Control
Frontotemporal dementia selectively impairs transitive reasoning about familiar spatial environments.	Data Not Reported
Frontotemporal dementia with the C9ORF72 hexanucleotide repeat expansion: clinical, neuroanatomical and neuropathological features.	Not bv

Frontotemporal lobar degeneration without lobar atrophy.	Not bv
Functional connectivity and microstructural white matter changes in phenocopy frontotemporal dementia.	Data Not Reported
Functional Connectivity Changes in Behavioral, Semantic, and Nonfluent Variants of Frontotemporal Dementia.	ROI
Functional Connectivity in Neurodegenerative Disorders: Alzheimer's Disease and Frontotemporal Dementia	Review Article
Functional dissociation between anterior temporal lobe and inferior frontal gyrus in the processing of dynamic body expressions: Insights from behavioral variant frontotemporal dementia.	Data Not Reported
Functional network connectivity in the behavioral variant of frontotemporal dementia.	ROI
Functional network resilience to pathology in presymptomatic genetic frontotemporal dementia	Not bv
Functional neural correlates of emotional expression processing deficits in behavioural variant frontotemporal dementia.	Data Not Reported
Functional overlap and divergence between ALS and bvFTD.	Data Not Reported
Globular glial tauopathy Type II: Clinicopathological study of two autopsy cases	Case Series
Gray and white matter changes in presymptomatic genetic frontotemporal dementia: a longitudinal MRI study	Not bv
Gray and white matter water diffusion in the syndromic variants of frontotemporal dementia.	11C-PiB PET Imaging
Grey and white matter changes across the amyotrophic lateral sclerosis-frontotemporal dementia continuum.	Data Not Reported
Hepatosplenomegaly, pneumopathy, bone changes and fronto-temporal dementia: Niemann-Pick type B and SQSTM1-associated Paget's disease in the same individual	Case Report
Heterogeneous brain FDG-PET metabolic patterns in patients with C9orf72 mutation	Not bv
Hierarchical organization of scripts: converging evidence from fMRI and frontotemporal degeneration.	ROI
Hippocampal atrophy on MRI in frontotemporal lobar degeneration and Alzheimer's disease.	Not bv
Hippocampal shape analysis in Alzheimer's disease and frontotemporal lobar degeneration subtypes.	ROI
Hippocampus and entorhinal cortex in frontotemporal dementia and Alzheimer's disease: a morphometric MRI study.	ROI
Homozygous sequestosome 1 (SQSTM1) mutation: a rare cause for childhood-onset progressive cerebellar ataxia with vertical gaze palsy	Irrelevant
Humour processing in frontotemporal lobar degeneration: A behavioural and neuroanatomical analysis	ROI
Imaging beta-amyloid burden in aging and dementia.	Not bv
Imaging signatures of molecular pathology in behavioral variant frontotemporal dementia.	Not bv
Impact of Imaging and Cerebrospinal Fluid Biomarkers on Behavioral Variant Frontotemporal Dementia Diagnosis within a Late-Onset Frontal Lobe Syndrome Cohort.	Irrelevant
Impaired acquisition rates of probabilistic associative learning in frontotemporal dementia is associated with fronto-striatal atrophy.	Not bv
Impaired Empathy Versus General Hypoemotionality in Frontotemporal Dementia	Cortical Volumes calculated by FreeSurfer
Impaired Recognition and Regulation of Disgust Is Associated with Distinct but Partially Overlapping Patterns of Decreased Gray Matter Volume in the Ventroanterior Insula.	Data Not Reported
Impaired recognition of body expressions in the behavioral variant of frontotemporal dementia.	Data Not Reported
Impairment of prosocial sentiments is associated with frontopolar and septal damage in frontotemporal dementia.	Data Not Reported
Improving response inhibition systems in frontotemporal dementia with citalopram.	Data Not Reported
In search of autobiographical memories: A PET study in the frontal variant of frontotemporal dementia.	Data Not Reported
In vivo amyloid imaging with PET in frontotemporal dementia.	11C-PiB PET Imaging
In vivo characterization of metabotropic glutamate receptor type 5 abnormalities in behavioral variant	Number of Patients Below 6

FTD.	
In vivo evidence of cortical amyloid deposition in the adult form of Niemann Pick type C	18F- Florbetaben PET Scan
In vivo staging of frontotemporal lobar degeneration TDP-43 type C pathology	Not bv
Individual patient diagnosis of AD and FTD via high-dimensional pattern classification of MRI.	Irrelevant
Individualized atrophy scores predict dementia onset in familial frontotemporal lobar degeneration	Not bv
Inheritance of the ApoE epsilon4 allele increases the rate of brain atrophy in dementia patients.	Not bv
Insight in frontotemporal dementia: conceptual analysis and empirical evaluation of the consensus criterion "loss of insight" in frontotemporal dementia.	Not bv
Investigation of (11)C-PiB equivocal PET findings.	ROI
Is hippocampal volume a good marker to differentiate Alzheimer's disease from frontotemporal dementia?	ROI
Joint assessment of structural, perfusion, and diffusion MRI in Alzheimer's disease and frontotemporal dementia	Data Not Reported
Joint assessment of white matter integrity, cortical and subcortical atrophy to distinguish AD from behavioral variant FTD: A two-center study.	Data Not Reported
Lateral Temporal Lobe: An Early Imaging Marker of the Presymptomatic GRN Disease?	Not bv
Lateralization on neuroimaging does not differentiate frontotemporal lobar degeneration from Alzheimer's disease.	Not bv
Left frontal lobe contributions to concept formation: a quantitative MRI study of performance on the Delis-Kaplan Executive Function System Sorting Test.	ROI
Lessons of the month 3: Spontaneous resolution of frontotemporal brain sagging syndrome	Case Report
Longitudinal ((18)F)AV-1451 PET imaging in a patient with frontotemporal dementia due to a Q351R MAPT mutation	Case Report
Longitudinal (18)F-FDG PET and MRI Reveal Evolving Imaging Pathology That Corresponds to Disease Progression in a Patient With ALS-FTD	Case Report
Longitudinal Amyloid- β PET in Atypical Alzheimer's Disease and Frontotemporal Lobar Degeneration	11C-PiB PET Imaging
Longitudinal analysis of brain atrophy in Alzheimer's disease and frontotemporal dementia	Case Series
Longitudinal grey and white matter changes in frontotemporal dementia and Alzheimer's disease.	ROI
Longitudinal Memory Profiles in Behavioral-Variant Frontotemporal Dementia and Alzheimer's Disease.	11C-PiB PET Imaging
Longitudinal neuroimaging and neuropsychological profiles of frontotemporal dementia with C9ORF72 expansions.	Not bv
Longitudinal patterns of regional change on volumetric MRI in frontotemporal lobar degeneration.	Not bv
Longitudinal rates of lobar atrophy in frontotemporal dementia, semantic dementia, and Alzheimer's disease.	No voxel-Based Morphometry Was Performed on MRI Images.
Longitudinal white matter changes in frontotemporal dementia subtypes.	Data Not Reported
Looking for Measures of Disease Severity in the Frontotemporal Dementia Continuum.	Not Case Control
Looking for Neuroimaging Markers in Frontotemporal Lobar Degeneration Clinical Trials: A Multi-Voxel Pattern Analysis Study in Granulin Disease.	Not bv
Loss of frontal fMRI activation in early frontotemporal dementia compared to early AD.	Not Case Control
Loss of insight and functional neuroimaging in frontotemporal dementia.	Not Case Control
Lost and forgotten? Orientation versus memory in Alzheimer's disease and frontotemporal dementia.	Data Not Reported
Magnetic resonance imaging and histopathology in dementia, clinically of frontotemporal type.	Not bv
Magnetic resonance imaging correlates of set shifting.	ROI
Magnetic resonance imaging in frontotemporal dementia shows subcortical atrophy.	ROI
Magnetic resonance imaging signatures of tissue pathology in frontotemporal dementia.	Not bv

Male gender is associated with greater cerebral hypometabolism in frontotemporal dementia: evidence for sex-related cognitive reserve.	Not Case Control
Measurements of the amygdala and hippocampus in pathologically confirmed Alzheimer disease and frontotemporal lobar degeneration.	Not bv
Measuring disease progression in frontotemporal lobar degeneration: a clinical and MRI study.	Irrelevant
Measuring network disruption in neurodegenerative diseases: New approaches using signal analysis	Review Article
Medial temporal lobe metabolic impairment in dementia associated with motor neuron disease.	Not bv
Medial versus lateral frontal lobe contributions to voluntary saccade control as revealed by the study of patients with frontal lobe degeneration.	Not bv
Memory consolidation and the hippocampus: further evidence from studies of autobiographical memory in semantic dementia and frontal variant frontotemporal dementia.	Number of Patients Below 6
Memory profiles in pathology or biomarker confirmed Alzheimer disease and frontotemporal dementia.	Number of Patients Below 6
Mentalising music in frontotemporal dementia.	ROI
Metabolic connectivity for differential diagnosis of dementing disorders.	Not bv
Mirror neurons and their relationship with neurodegenerative disorders	Not bv
Money for nothing - Atrophy correlates of gambling decision making in behavioural variant frontotemporal dementia and Alzheimer's disease	Data Not Reported
Moral processing deficit in behavioral variant frontotemporal dementia is associated with facial emotion recognition and brain changes in default mode and salience network areas	Data Not Reported
More atrophy of deep gray matter structures in frontotemporal dementia compared to Alzheimer's disease.	Not bv
Motor speech signature of behavioral variant frontotemporal dementia: Refining the phenotype.	ROI
MR analysis of the substantia innominata in normal aging, Alzheimer disease, and other types of dementia.	Not bv
MRI correlates of protein deposition and disease severity in postmortem frontotemporal lobar degeneration.	Data Not Reported
MRI of the Swallow Tail Sign: A Useful Marker in the Diagnosis of Lewy Body Dementia?	Irrelevant
MRI patterns of atrophy and hypoperfusion associations across brain regions in frontotemporal dementia.	Deformation-based morphometry (DBM)
MRI signatures of brain macrostructural atrophy and microstructural degradation in frontotemporal lobar degeneration subtypes.	Data Not Reported
MRI signatures of the frontotemporal lobar degeneration continuum.	Data Not Reported
MRI visual rating scales in the diagnosis of dementia: evaluation in 184 post-mortem confirmed cases.	Not bv
Multicenter standardized 18F-FDG PET diagnosis of mild cognitive impairment, Alzheimer's disease, and other dementias.	Not bv
Multimodal fMRI resting-state functional connectivity in granulin mutations: the case of fronto-parietal dementia.	Not bv
Multimodal MRI of grey matter, white matter, and functional connectivity in cognitively healthy mutation carriers at risk for frontotemporal dementia and Alzheimer's disease	Not bv
Multimodal MRI quantification of the common neurostructural bases within the FTD-ALS continuum.	Data Not Reported
Multiparametric computer-aided differential diagnosis of Alzheimer's disease and frontotemporal dementia using structural and advanced MRI.	Not bv
Multiparametric MRI to distinguish early onset Alzheimer's disease and behavioural variant of frontotemporal dementia.	Not Case Control
Music recognition in frontotemporal lobar degeneration and Alzheimer disease.	Data Not Reported
My belief or yours? Differential theory of mind deficits in frontotemporal dementia and Alzheimer's disease.	Data Not Reported
Naming and conceptual understanding in frontotemporal dementia	Not Case Control
Network degeneration and dysfunction in presymptomatic C9ORF72 expansion carriers.	Irrelevant

Network-selective vulnerability of the human cerebellum to Alzheimer's disease and frontotemporal dementia.	ROI
Neural basis of interpersonal traits in neurodegenerative diseases.	Data Not Reported
Neural basis of motivational approach and withdrawal behaviors in neurodegenerative disease	Data Not Reported
Neural correlates of activities of daily living in frontotemporal dementia.	Not bv
Neural correlates of behavioural symptoms in behavioural variant frontotemporal dementia and Alzheimer's disease: Employment of a visual MRI rating scale.	Irrelevant
Neural correlates of caregiver burden in cortical basal syndrome and frontotemporal dementia.	Data Not Reported
Neural correlates of empathic impairment in the behavioral variant of frontotemporal dementia.	Data Not Reported
Neural correlates of episodic memory in behavioral variant frontotemporal dementia.	No voxel-Based Morphometry Was Performed on MRI Images.
Neural correlates of reduced awareness in instrumental activities of daily living in frontotemporal dementia.	Data Not Reported
Neural correlates of semantic and behavioural deficits in frontotemporal dementia.	Not bv
Neural correlates of the DemTect in Alzheimer's disease and frontotemporal lobar degeneration - A combined MRI & FDG-PET study.	Data Not Reported
Neural substrates of episodic memory dysfunction in behavioural variant frontotemporal dementia with and without C9ORF72 expansions	Data Not Reported
Neural substrates of socioemotional self-awareness in neurodegenerative disease	Data Not Reported
Neuroanatomical correlates of emotional blunting in behavioral variant frontotemporal dementia and early-onset Alzheimer's disease.	Tensor-based Morphometry (TBM)
Neuroanatomical profiles of personality change in frontotemporal lobar degeneration.	Data Not Reported
Neuroanatomy of apathy and disinhibition in frontotemporal lobar degeneration.	Not bv
Neuroanatomy of the self: evidence from patients with frontotemporal dementia.	Not Case Control
Neurodegeneration Behind Bars: From molecules to jurisprudence	Review Article
Neuroeconomic dissociation of semantic dementia and behavioural variant frontotemporal dementia	Data Not Reported
Neuroimaging Correlates of Frontotemporal Dementia Associated with SQSTM1 Mutations.	Not bv
Neuroimaging in dementia.	Review Article
Neuroimaging in the diagnosis of frontotemporal dementia.	Irrelevant
Neuroimaging of Diseases Causing Dementia	Review Article
Neuroimaging of Inflammation in Memory and Related Other Disorders (NIMROD) study protocol: a deep phenotyping cohort study of the role of brain inflammation in dementia, depression and other neurological illnesses.	Irrelevant
Neuroimaging patterns along the ALS-FTD spectrum: a multiparametric imaging study.	Data Not Reported
Neuroimaging signatures of frontotemporal dementia genetics: C9ORF72, tau, progranulin and sporadics.	Data Not Reported
Neuroinflammation and protein aggregation co-localize across the frontotemporal dementia spectrum	11C-PK-11195 PET scanning
Neuropsychiatric effects of neurodegeneration of the medial versus lateral ventral prefrontal cortex in humans.	Not bv
Neuropsychological and Neuroanatomical Correlates of the Social Norms Questionnaire in Frontotemporal Dementia Versus Alzheimer's Disease.	Not Case Control
Niemann-Pick Disease Type C Misdiagnosed as Cerebral Palsy: A Case Report	Case Report
Novel cerebrospinal fluid biomarkers of axonal degeneration in frontotemporal dementia.	Not bv
Occupational attainment influences longitudinal decline in behavioral variant frontotemporal degeneration	Data Not Reported
Olfactory function in corticobasal syndrome and frontotemporal dementia.	ROI
Open-label study of the short-term effects of memantine on FDG-PET in frontotemporal dementia.	Data Not Reported

Overlap in frontotemporal atrophy between normal aging and patients with frontotemporal dementias.	ROI
Pain and temperature processing in dementia: a clinical and neuroanatomical analysis.	Not bv
Pain Anticipation and Nocebo-Related Responses: A Descriptive Mini-Review of Functional Neuroimaging Studies in Normal Subjects and Precious Hints on Pain Processing in the Context of Neurodegenerative Disorders	Review Article
Pathophysiology of the behavioral variant of frontotemporal lobar degeneration: A study combining MRI and FDG-PET	ROI
Pattern of glucose hypometabolism in frontotemporal dementia with motor neuron disease.	Not bv
Patterns of atrophy in pathologically confirmed dementias: a voxelwise analysis.	Irrelevant
Patterns of atrophy in pathologically confirmed FTLT with and without motor neuron degeneration.	Not bv
Patterns of brain atrophy in clinical variants of frontotemporal lobar degeneration.	Not Case Control
Patterns of brain atrophy in frontotemporal dementia and semantic dementia.	Data Not Reported
Patterns of cortical thinning in Alzheimer's disease and frontotemporal dementia.	No voxel-Based Morphometry Was Performed on MRI Images.
Patterns of frontal lobe atrophy in frontotemporal dementia: a volumetric MRI study.	ROI
Patterns of gray matter atrophy in genetic frontotemporal dementia: results from the GENFI study.	Not bv
Patterns of MRI atrophy in tau positive and ubiquitin positive frontotemporal lobar degeneration.	Not bv
Patterns of regional cerebellar atrophy in genetic frontotemporal dementia.	Not bv
Patterns of striatal degeneration in frontotemporal dementia.	ROI
Patterns of white matter atrophy in frontotemporal lobar degeneration.	No voxel-Based Morphometry Was Performed on MRI Images.
Phenotype variability in progranulin mutation carriers: a clinical, neuropsychological, imaging and genetic study.	Irrelevant
Pittsburgh compound B imaging and cerebrospinal fluid amyloid- β in a multicentre European memory clinic study.	¹¹ C-PiB PET Imaging
Posterior cerebral atrophy in the absence of medial temporal lobe atrophy in pathologically-confirmed Alzheimer's disease.	Not bv
Predominant subcortical accumulation of (18)F-flortaucipir binding in behavioral variant frontotemporal dementia.	ROI
Profiles of white matter tract pathology in frontotemporal dementia.	Data Not Reported
Prognosis of Patients with Behavioral Variant Frontotemporal Dementia Who have Focal Versus Diffuse Frontal Atrophy.	Irrelevant
Progression of logopenic aphasia to frontotemporal dementia in an amyloid β -negative and (18) F-THK-5351-positive patient	Case Report
Progressive brainstem pathology in motor neuron diseases: Imaging data from amyotrophic lateral sclerosis and primary lateral sclerosis	Irrelevant
Prominent auditory deficits in primary progressive aphasia: A case study	Case Report
Prosocial deficits in behavioral variant frontotemporal dementia relate to reward network atrophy.	Data Not Reported
Putaminal volume in frontotemporal lobar degeneration and Alzheimer disease: differential volumes in dementia subtypes and controls.	ROI
Qualitative Assessment of Longitudinal Changes in Phenocopy Frontotemporal Dementia	Not bv
Quantifying change in individual subjects affected by frontotemporal lobar degeneration using automated longitudinal MRI volumetry.	ROI
Quantitative analysis of grey matter degeneration in FTD patients using fractal dimension analysis.	No voxel-Based Morphometry Was Performed on MRI Images.
Quantitative validation of a visual rating scale for frontal atrophy: associations with clinical status, APOE e4, CSF biomarkers and cognition.	Irrelevant
Rates of brain atrophy over time in autopsy-proven frontotemporal dementia and Alzheimer disease.	Not bv

Rates of global and regional cerebral atrophy in AD and frontotemporal dementia.	No voxel-Based Morphometry Was Performed on MRI Images.
Rates of lobar atrophy in asymptomatic MAPT mutation carriers	Not bv
Re-evaluation of clinical dementia diagnoses with pittsburgh compound B positron emission tomography.	Not Case Control
Recommendations to distinguish behavioural variant frontotemporal dementia from psychiatric disorders	Review Article
Reduced cortical thickness in the posterior cingulate gyrus is characteristic of both typical and atypical Alzheimer's disease.	Number of Patients Below 6
Reduced precuneus deactivation during object naming in patients with mild cognitive impairment, Alzheimer's disease, and frontotemporal lobar degeneration	Data Not Reported
Region-specific decline of cerebral glucose metabolism in patients with frontotemporal dementia: a prospective 18F-FDG-PET study.	Data Not Reported
Regional cerebral blood flow correlates eating abnormalities in frontotemporal dementia	Not Case Control
Regional differences in white matter breakdown between frontotemporal dementia and early-onset Alzheimer's disease.	DWI
Registration accuracy for VBM studies varies according to region and degenerative disease grouping.	Irrelevant
Relationship between occupation attributes and brain metabolism in frontotemporal dementia.	Not Case Control
Relevance of raised cerebrospinal fluid monocyte levels in patients with frontotemporal dementia.	Data Not Reported
Resting parasympathetic dysfunction predicts prosocial helping deficits in behavioral variant frontotemporal dementia	Data Not Reported
Resting State Dynamic Functional Connectivity in Neurodegenerative Conditions: A Review of Magnetic Resonance Imaging Findings	Review Article
Resting state functional connectivity differences between behavioral variant frontotemporal dementia and Alzheimer's disease	Data Not Reported
Reward deficits in behavioural variant frontotemporal dementia include insensitivity to negative stimuli.	ROI
Right anterior temporal lobe dysfunction underlies theory of mind impairments in semantic dementia	Irrelevant
Right Limbic FDG-PET Hypometabolism Correlates with Emotion Recognition and Attribution in Probable Behavioral Variant of Frontotemporal Dementia Patients.	No Controls
Role of right pregenual anterior cingulate cortex in self-conscious emotional reactivity.	VOI
Role of semiquantitative assessment of regional binding potential in 123I-FP-CIT SPECT for the differentiation of frontotemporal dementia, dementia with Lewy bodies, and Alzheimer's dementia.	Not bv
Saccade abnormalities in autopsy-confirmed frontotemporal lobar degeneration and Alzheimer disease.	Not bv
Saccadic abnormalities in frontotemporal dementia.	Data Not Reported
Salience network resting-state activity: prediction of frontotemporal dementia progression.	Number of Patients Below 6
Schizophrenia Phenotype Preceding Behavioral Variant Frontotemporal Dementia Related to C9orf72 Repeat Expansion	Case Report
Self-awareness in neurodegenerative disease relies on neural structures mediating reward-driven attention.	Data Not Reported
Serotonin-1A receptors in frontotemporal dementia compared with controls.	Number of Patients Below 6
Shape analysis of the neostriatum in subtypes of frontotemporal lobar degeneration: neuroanatomically significant regional morphologic change.	Volumetric Analysis
Simple linear and area MR measurements can help distinguish between Alzheimer's disease, frontotemporal dementia, and normal aging: the Sunnybrook dementia study.	paper and abstract not available
Single Subject Classification of Alzheimer's Disease and Behavioral Variant Frontotemporal Dementia Using Anatomical, Diffusion Tensor, and Resting-State Functional Magnetic Resonance Imaging.	Data Not Reported
Social and cognitive control skills in long-life occupation activities modulate the brain reserve in the behavioural variant of frontotemporal dementia.	Not Case Control
Social Cognition and Emotional Assessment (SEA) is a marker of medial and orbital frontal functions: a voxel-based morphometry study in behavioral variant of frontotemporal degeneration.	ROI

Social cognition, executive functioning, and neuroimaging correlates of empathic deficits in frontotemporal dementia.	Data Not Reported
Social conceptual impairments in frontotemporal lobar degeneration with right anterior temporal hypometabolism.	Not bv
Social mind representation: where does it fail in frontotemporal dementia?	Data Not Reported
Spatiotemporal analysis for detection of pre-symptomatic shape changes in neurodegenerative diseases: Initial application to the GENFI cohort	Not bv
Striatal Atrophy in the Behavioural Variant of Frontotemporal Dementia: Correlation with Diagnosis, Negative Symptoms and Disease Severity.	ROI
Striatal dopamine transporter and extrapyramidal symptoms in frontotemporal dementia.	ROI
Structural anatomy of empathy in neurodegenerative disease.	Data Not Reported
Structural and functional brain abnormalities place phenocopy frontotemporal dementia (FTD) in the FTD spectrum.	ROI
Structural MRI in frontotemporal dementia: comparisons between hippocampal volumetry, tensor-based morphometry and voxel-based morphometry.	ROI
Structural neuroanatomy of face processing in frontotemporal lobar degeneration.	Data Not Reported
Structural neuroimaging of social cognition in progressive non-fluent aphasia and behavioral variant of frontotemporal dementia.	Not bv
Subacute combined degeneration of the spinal cord masking motor neuron disease: a case report	Case Report
Subcortical and Deep Cortical Atrophy in Frontotemporal Dementia due to Granulin Mutations.	Not bv
Subcortical atrophy in frontotemporal dementia and Alzheimer's disease: Significance for the differential diagnosis and correlations with clinical manifestations.	No voxel-Based Morphometry Was Performed on MRI Images.
Survival in frontotemporal lobar degeneration and related disorders: Latent class predictors and brain functional correlates	Irrelevant
Tackling variability: A multicenter study to provide a gold-standard network approach for frontotemporal dementia.	Connectivity Matrices
Tau forms in CSF as a reliable biomarker for progressive supranuclear palsy.	Irrelevant
Tau haplotype influences cerebral perfusion pattern in frontotemporal lobar degeneration and related disorders.	99mTc-ECD SPECT acquisition
TDP-43 subtypes are associated with distinct atrophy patterns in frontotemporal dementia.	Not bv
Temporal lobe rating scale: application to Alzheimer's disease and frontotemporal dementia.	ROI
Temporal variant of frontotemporal dementia in C9orf72 repeat expansion carriers: two case studies	Case Series
Temporoparietal atrophy: a marker of AD pathology independent of clinical diagnosis.	Not bv
Temporoparietal hypometabolism in frontotemporal lobar degeneration and associated imaging diagnostic errors.	Not bv
Thalamic nuclei in frontotemporal dementia: Mediodorsal nucleus involvement is universal but pulvinar atrophy is unique to C9orf72	ROI
The 5-HTTLPR variant in the serotonin transporter gene modifies degeneration of brain regions important for emotion in behavioral variant frontotemporal dementia.	Data Not Reported
The added value of 18-fluorodeoxyglucose-positron emission tomography in the diagnosis of the behavioral variant of frontotemporal dementia.	Irrelevant
The Association Between Distinct Frontal Brain Volumes and Behavioral Symptoms in Mild Cognitive Impairment, Alzheimer's Disease, and Frontotemporal Dementia	ROI
The attribution of animacy and agency in frontotemporal dementia versus Alzheimer's disease.	ROI
The behavioural/dysexecutive variant of Alzheimer's disease: clinical, neuroimaging and pathological features.	Irrelevant
The brain basis of musicophilia: evidence from frontotemporal lobar degeneration.	Not bv
The Cerebellum in Frontotemporal Dementia: a Meta-Analysis of Neuroimaging Studies	Meta-Analysis
The clinical and anatomical heterogeneity of environmental dependency phenomena.	Data Not Reported

The correlation of cognitive decline with frontotemporal dementia induced annualized gray matter loss using diffeomorphic morphometry.	Not bv
The Evolution of Caregiver Burden in Frontotemporal Dementia with and without Amyotrophic Lateral Sclerosis.	Not Case Control
The frontal-anatomic specificity of design fluency repetitions and their diagnostic relevance for behavioral variant frontotemporal dementia.	Irrelevant
The inner fluctuations of the brain in presymptomatic Frontotemporal Dementia: The chronnectome fingerprint	Not bv
The Italian Alzheimer's Disease Neuroimaging Initiative (I-ADNI): validation of structural MR imaging.	Irrelevant
The Language Profile of Behavioral Variant Frontotemporal Dementia.	Data Not Reported
The longitudinal decline of white matter microstructural integrity in behavioral variant frontotemporal dementia and its association with executive function	DWI
The longitudinal evaluation of familial frontotemporal dementia subjects protocol: Framework and methodology	Protocol Article
The neural basis for establishing a focal point in pure coordination games.	Volumetric MRI
The neural correlates and clinical characteristics of psychosis in the frontotemporal dementia continuum and the C9orf72 expansion.	Data Not Reported
The orbitofrontal cortex is involved in emotional enhancement of memory: evidence from the dementias.	ROI
The Phenotype of the C9ORF72 Expansion Carriers According to Revised Criteria for bvFTD.	Not Case Control
The power of neuroimaging biomarkers for screening frontotemporal dementia.	Volumetric MRI and DWI
The role of MAPT gene in Chinese dementia patients: A P301I pedigree study and brief literature review	No Control
The structural neuroanatomy of music emotion recognition: evidence from frontotemporal lobar degeneration.	Data Not Reported
The tauopathy associated with mutation +3 in intron 10 of Tau: characterization of the MSTD family.	Not bv
The underlying mechanisms of verbal fluency deficit in frontotemporal dementia and semantic dementia.	Data Not Reported
The Use of Biomarkers and Genetic Screening to Diagnose Frontotemporal Dementia: Evidence and Clinical Implications	Review Article
The value of FDG-PET/CT by using 3-dimensional stereotactic surface projection software analysis in the differential diagnosis of dementia.	Not bv
Theory of mind impairment in patients with behavioural variant fronto-temporal dementia (bv-FTD) increases caregiver burden.	Data Not Reported
Topographical patterns of lobar atrophy in frontotemporal dementia and Alzheimer's disease.	Not bv
Topography of primitive reflexes in dementia: an F-18 fluorodeoxyglucose positron emission tomography study.	Not bv
Trajectories of brain and hippocampal atrophy in FTD with mutations in MAPT or GRN.	Not bv
Trajectory of lobar atrophy in asymptomatic and symptomatic GRN mutation carriers: a longitudinal MRI study	Not bv
Two distinct subtypes of right temporal variant frontotemporal dementia.	Not bv
Typical cerebral metabolic patterns in neurodegenerative brain diseases.	Not bv
Unified voxel- and tensor-based morphometry (UVTBM) using registration confidence.	Not bv
Urinary incontinence and its functional anatomy in frontotemporal lobar degenerations.	Not bv
Usefulness of measurement of the temporal stem on magnetic resonance imaging in the diagnosis of frontotemporal dementia.	Not bv
Using simultaneous PET/MRI to compare the accuracy of diagnosing frontotemporal dementia by arterial spin labelling MRI and FDG-PET.	Not bv
Validating FDG-PET as a biomarker for frontotemporal dementia.	Irrelevant
Validation of consensus panel diagnosis in dementia.	Irrelevant
Validation of the Spanish version of the Addenbrooke's Cognitive Examination in a rural community in	Irrelevant

Spain.	
Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia.	Irrelevant
Variant-specific vulnerability in metabolic connectivity and resting-state networks in behavioural variant of frontotemporal dementia	Data Not Reported
VBM signatures of abnormal eating behaviours in frontotemporal lobar degeneration.	Not bv
Ventricular volume expansion in presymptomatic genetic frontotemporal dementia	Not bv
Ventromedial-frontopolar prefrontal cortex atrophy correlates with insight loss in frontotemporal dementia and Alzheimer's disease.	Not Case Control
Visual assessment of atrophy on magnetic resonance imaging in the diagnosis of pathologically confirmed young-onset dementias.	Irrelevant
Visual perceptual organization deficits in Alzheimer's dementia.	Number of Patients Below 6
Visual rating and volumetry of the medial temporal lobe on magnetic resonance imaging in dementia: a comparative study.	Irrelevant
Visual search patterns in semantic dementia show paradoxical facilitation of binding processes.	ROI
Visuospatial dysfunction in Alzheimer's disease and behavioural variant frontotemporal dementia	11C-PiB PET Imaging
Volumetric study of lobar atrophy in Pick complex and Alzheimer's disease.	No voxel-Based Morphometry Was Performed on MRI Images.
Voxel-based classification of FDG PET in dementia using inter-scanner normalization.	Irrelevant
Voxel-based morphometry in frontotemporal lobar degeneration with ubiquitin-positive inclusions with and without progranulin mutations.	Not bv
Voxel-based morphometry in patients with obsessive-compulsive behaviors in behavioral variant frontotemporal dementia.	Data Not Reported
Voxel-based morphometry in tau-positive and tau-negative frontotemporal lobar degenerations.	Not bv
Voxel-based morphometry patterns of atrophy in FTLT with mutations in MAPT or PGRN	Not bv
When one loses empathy: its effect on carers of patients with dementia.	Irrelevant
White Matter Changes Associated with Resting Sympathetic Tone in Frontotemporal Dementia vs. Alzheimer's Disease.	Cortical volumes calculated by FreeSurfer and DWI
White matter damage in frontotemporal dementia and Alzheimer's disease measured by diffusion MRI.	DWI
White matter damage in frontotemporal lobar degeneration spectrum.	ROI
White matter disease contributes to apathy and disinhibition in behavioral variant frontotemporal dementia.	DWI
White matter tract signatures of impaired social cognition in frontotemporal lobar degeneration.	DWI
Why are patients with progressive nonfluent aphasia nonfluent?	No voxel-Based Morphometry Was Performed on MRI Images.

Supplementary references

1. Lee, S.E., et al., *Altered network connectivity in frontotemporal dementia with C9orf72 hexanucleotide repeat expansion*. Brain, 2014. **137**(Pt 11): p. 3047-60.
2. Seeley, W.W., et al., *Frontal paralimbic network atrophy in very mild behavioral variant frontotemporal dementia*. Arch Neurol, 2008. **65**(2): p. 249-55.
3. Mandelli, M.L., et al., *Two insular regions are differentially involved in behavioral variant FTD and nonfluent/agrammatic variant PPA*. Cortex, 2016. **74**: p. 149-57.
4. Agosta, F., et al., *Apolipoprotein E epsilon4 is associated with disease-specific effects on brain atrophy in Alzheimer's disease and frontotemporal dementia*. Proc Natl Acad Sci U S A, 2009. **106**(6): p. 2018-22.
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