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Frontotemporal dementia, music perception and social cognition share neurobiological circuits: A meta-analysis

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ABSTRACT

Frontotemporal dementia (FTD) is a neurodegenerative disease that presents with profound changes in social cognition. Music might be a sensitive probe for social cognition abilities, but underlying neurobiological substrates are unclear. We performed a meta-analysis of voxel-based morphometry studies in FTD patients and functional MRI studies for music perception and social cognition tasks in cognitively normal controls to identify robust patterns of atrophy (FTD) or activation (music perception or social cognition). Conjunction analyses were performed to identify overlapping brain regions. In total 303 articles were included: 53 for FTD (n = 1153 patients, 42.5% female; 1337 controls, 53.8% female), 28 for music perception (n = 540, 51.8% female) and 222 for social cognition in controls (n = 5664, 50.2% female). We observed considerable overlap in atrophy patterns associated with FTD, and functional activation associated with music perception and social cognition, mostly encompassing the ventral language network. We further observed overlap across all three modalities in mesolimbic, basal forebrain and striatal regions. The results of our meta-analysis suggest that music perception and social cognition share neurobiological circuits that are affected in FTD. This supports the idea that music might be a sensitive probe for social cognition abilities with implications for diagnosis and monitoring.

1. Introduction

Frontotemporal dementia (FTD) is a neurodegenerative disease characterized by frontal and temporal lobar degeneration. It is the second most prevalent cause of early-onset dementia following Alzheimer's disease (Harvey et al. 2003; Ratnavalli et al. 2002). Contrary to other types of dementia, personality change and behavioral abnormalities are characteristics of FTD, which can occur even in the absence of cognitive decline. Since FTD is highly heterogeneous, both clinically and pathologically, it often poses a diagnostic challenge (Rascovsky et al. 2011). An early hallmark of FTD is a loss of appropriate interpersonal conduct due to a decline in social cognition abilities (Adenzato et al. 2010; Piguet et al. 2011). Social cognition is a multi-componential term used to describe cognitive processes related to the perception, understanding, and implementation of social cues (Van Overwalle et al. 2015; Suchy and Holdnack 2013) and comprises abilities such as emotion recognition, mentalizing (or Theory of Mind) and empathy. Impairment of social cognition is not specific for FTD (Agustus et al. 2015; Bora et al. 2016; Gossink et al. 2018), as it is also a key symptom of psychiatric disorders such as autism and schizophrenia (Baron-Cohen et al. 2000; Corcoran et al. 1995; Langdon et al. 2002), and several acute neurological disorders (Buunk et al. 2017; May et al. 2017; Nijsse et al. 2019; Xiao et al. 2017). Despite the fact that social cognitive impairments are core symptoms in FTD (Rascovsky et al. 2011), and result in increased caregiver burden (Guevara et al. 2015; Hsieh et al. 2013), as of yet there is no gold standard for measuring social cognition abilities in the context of FTD diagnostics. On the other hand, FTD is a neuroanatomically well-defined disorder and as such may serve as a neurobiological model to understand the complex system involved in social cognition. Improved understanding of the neurobiological basis involved in social cognition and its impairment in FTD might aid in developing diagnostic tools across illness and disorders.

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Music is suggested to be a sensitive probe for social cognition abilities (Clark et al. 2014, 2015; Downey et al. 2013; P. D. Fletcher et al. 2013); various studies have found that both emotional music processing and social cognition are disturbed in FTD. For example, Downey et al. found that FTD patients have a specific inability to attribute mental states to music ('musical mentalising'), which correlated with tested performance on social cognition (TASIT) and reported empathy (Downey et al. 2013). Furthermore, brain regions involved in music emotion-recognition were found to be involved in Theory of Mind in FTD, which suggests a shared neurobiological circuit (Omar et al. 2011). Case-reports and explorative imaging studies also suggest that music perception, just like social cognition, is altered in patients with FTD, with patients and caregivers reporting changes in music perception, varying from musicophilia (enhanced appreciation of music) (Fletcher et al. 2013) to change of musical taste (Boeve and Geda 2001; Fletcher et al. 2013; Geroldi et al. 2000; Sacks 2007) and sound-aversion (Hardy et al. 2016). One study found worse performance on social cognition abilities in FTD patients with musicophilia (Fletcher et al. 2013). As such it could be hypothesized that music perception shares neurobiological correlates with social cognition and brain areas affected in FTD. So far, research has mostly investigated atrophy in FTD and functional activity in social cognition and music perception separately. In FTD a network is affected which includes frontoinsular, cingulate and striatal structures (Seeley et al. 2009; Zhou et al. 2010); in music perception the temporal cortices and various frontal regions were identified (Janata 2015; Limb 2006); and in social cognition various frontal, temporal and parietal brain regions are identified (Molenberghs et al. 2016; Schurz et al. 2014). Studies that investigated neural substrates for social cognition in FTD patients demonstrated associations with fronto-insulo-temporal atrophy (Couto et al. 2013; Eslinger et al. 2011). We hypothesized that these circuits of atrophy in FTD are also involved in music perception. More specifically, that these circuits would be most affected in FTD subtypes in whom behavioral symptoms would be most prominent. Furthermore, we hypothesized that social cognition subcomponents empathy and Theory of Mind would involve specific brain regions within this circuit.

In this meta-analysis we investigated whether brain areas showing atrophy in FTD show anatomical overlap with brain areas that are normally activated during music perception and social cognition tasks to investigate shared neurobiological circuits. Furthermore, we performed subgroup analyses in FTD and social cognition to specify for FTD subtypes and social cognition subcomponents.

2. Methods and materials

2.1. Literature search and screening strategy

The PRISMA guideline was used to perform this meta-analysis (Moher et al. 2009). The literature search was performed in April 2020. A search and selection of papers was conducted in the BrainMap database using Sleuth 3.0.3 software (Fox et al. 2005; Fox and Lancaster 2002; Laird et al. 2005) and in PubMed and Google Scholar. BrainMap is a database where MRI scan results are stored of both functional and structural neuroimaging studies (Fox and Lancaster 2002). Articles and experiments selection were performed with Sleuth 3.0.3, which is the search engine of BrainMap. Additional imaging coordinates of results from the PubMed and Google Scholar searches were manually added for inclusion in this meta-analysis. Separate literature searches were performed on the topics 'frontotemporal dementia', 'social cognition' and 'music perception'. Below we discuss the search and screening process of these topics in more detail for each modality. Papers were included when (a) structural studies compared patients with frontotemporal dementia with cognitively normal controls; (b) functional studies included subjects with normal vision, audition for music perception and without psychiatric or neurological diseases for music perception and social cognition (c) whole-brain unbiased voxelwise analysis was performed; (e) stereotaxic coordinates in Talairach or Montreal Neurological Institute (MNI) coordinates were reported; (f) articles were written in English. For a full overview of the selection process see the flowcharts in the supplemental material.

2.2. Frontotemporal dementia

To determine which brain areas show atrophy in frontotemporal dementia a search was conducted in BrainMap's Voxel-Based Morphometry database. We selected articles archived under the paradigm frontotemporal dementia (Subject > Diagnosis > is > Frontotemporal Dementia: 15 papers), frontotemporal lobar degeneration (Subject > Diagnosis > is > Frontotemporal Lobar Degeneration: 12 papers), semantic dementia (Subject > Diagnosis > is > Semantic Dementia: 8 papers) and progressive nonfluent aphasia (Subject > Diagnosis > is > Progressive Nonfluent Aphasia: 9 papers). All FTD subtypes were included. This resulted in 14 articles for inclusion. A manual search in PubMed and Google Scholar was performed using the terms 'Voxel-based morphometry'; 'VBM'; 'semantic dementia'; 'primary progressive nonfluent aphasia'; 'frontotemporal dementia'; 'frontotemporal lobar degeneration'; 'FTD' and 'FTLD' and resulted in 44 additional articles for inclusion. Papers from the same patient cohort were excluded.

2.3. Music perception

To determine which brain areas are activated during music perception tasks a search was conducted in the functional BrainMap database. We selected articles archived under the experimental paradigm music comprehension (Experiments > Paradigm Class > is > Music Comprehension: 65 papers) and passive listening (Experiments > Paradigm Class > is > Passive Listening: 113 papers). This resulted in 9 articles for inclusion. A manual search on PubMed and Google Scholar was performed using the terms 'magnetic resonance imaging'; 'MRI'; 'fMRI'; 'music perception'; 'music comprehension' and 'music processing' and resulted in 19 additional papers for inclusion.

2.4. Social cognition

To determine which brain areas are activated during social cognition tasks a search was conducted in the functional BrainMap database. We selected articles archived under the experimental paradigm 'Theory of Mind' (Experiments > Paradigm Class > is > Theory of Mind: 86 papers), 'Social Cognition' (Experiments > Behavioral domain > is > Cognition > Social Cognition: 127 papers) and body language perception (Experiments > Paradigm Class > is > Emotional Body Language Perception: 8 papers). This resulted in 17 articles for inclusion. A manual search in PubMed and Google Scholar was performed using the terms 'magnetic resonance imaging'; 'MRI'; 'fMRI'; 'social cognition'; 'theory of mind'; 'perspective taking'; 'mentalizing'; 'mentalising'; 'empathy'; 'emotion recognition' and 'emotion perception' and resulted in 205 additional articles for inclusion.

2.5. Statistical analyses

The meta-analysis was carried out in BrainMap's GingerALE 3.0.2 (http://brainmap.org/ale/index.html). The procedure was as follows: (1) All coordinates were converted to Talairach space using the Lancaster transformation before being entered into the analysis (Lancaster et al. 2007). (2) Activation Likelihood Estimate (ALE) meta-analysis calculations were performed (Simon B. Eickhoff et al. 2009; Simon B Eickhoff et al. 2012; Turkeltaub et al. 2012). Activation foci in a given experiment are combined for each voxel, resulting in a modeled activation map that describes the convergence of results of sets of voxels in the brain. (3) Thresholding of the ALE scores based on the null-hypothesis (Simon B Eickhoff et al. 2012).

First, we examined modality specific effects of patterns of atrophy involved in FTD and functional activation in cognitive normal subjects (music perception and social cognition). We performed three pairwise conjunction analyses to study the overlap between: 1. FTD and music perception; 2. FTD and social cognition; 3. Music perception and social cognition. Finally, we performed subgroup analyses on FTD subtypes (bvFTD, semantic dementia, progressive nonfluent aphasia) to study whether results were specific to any subtype, and we repeated analyses on social cognition including only studies on empathy and Theory of Mind to investigate how these studies influence the results. Statistical maps were thresholded using cluster-level family-wise error (FWE) correction $P < 0.05$ (S.B. Eickhoff et al. 2012).

3. Results

Our search terms resulted in a total of 3290 articles of which 369 for FTD, 685 for music perception and 2236 for social cognition. Fifty-three articles met the inclusion criteria for FTD, 28 for music perception and 222 for social cognition and were subjected to meta-analysis (Flowcharts 1, 2, 3 in the supplementary material), including a total of 8694 subjects: 1153 with FTD, 1337 controls (881 foci; Table 1; Table S1), 540 cognitively normal subjects for music perception (539 foci; Table 2; Table S2) and 5664 cognitively normal subjects for social cognition (3421 foci; Table 3; Table S3). Participants with FTD showed a slightly higher proportion of males whereas the controls were evenly distributed (42.5% and 53.8% female). Gender was evenly distributed amongst participants in music perception (51.8% female) and social cognition studies (50.2% female).

3.1. Modality specific meta-analytic results

3.1.1. Frontotemporal dementia atrophy correlates

The meta-analysis showed atrophy in FTD involving frontal structures such as the inferior, middle and superior frontal gyri, anterior cingulate gyri, temporal structures such as the insula, inferior, middle and superior temporal gyri and subcortical regions such as the amygdala and striatum (Fig. 1; Table S4). Repeating analyses separately for FTD subtypes, we observed specific bilateral frontoinsular and striatal atrophy patterns in bvFTD and semantic dementia and left-sided atrophy in PNFA. Additionally, bvFTD and semantic dementia showed atrophy in the amygdalae. Semantic dementia and PNFA showed atrophy of the superior and middle temporal gyri (Fig. S1-3; Table S5-7).

3.1.2. Music perception correlates

Functional activation during music perception involved the superior and middle temporal gyri, insula, middle and inferior frontal gyri, right thalamus, hypothalamus and striatum (Fig. 1; Table S8).

3.1.3. Social cognition correlates

Functional activation during social cognition tasks involved the superior, middle and inferior temporal gyri, insula, superior, middle and inferior frontal gyri, amygdala, thalamus, striatum and anterior cingulate cortex (Fig. 1; Table S9). Repeating analyses for empathy showed activation patterns in the insulae extending to the inferior frontal gyrus, striatum, thalami, amygdala and brainstem, the caudal temporal cortices and right postcentral gyrus (Figure S4; Table S10). Repeating analyses for Theory of Mind showed activation patterns in the bilateral temporo-parietal junction extending to the inferior frontal gyrus and precentral gyrus, precuneus, ventromedial prefrontal cortex and left striatum (Figure S4; Table S11).

3.1.4. Conjunction analyses

All conjunction analyses showed involvement of a pathway extending from the temporal cortex (BA 21, 22) through the insula (BA 13) to the inferior frontal gyri (BA 47). Additionally, basal forebrain, striatal and mesolimbic regions were activated on the right side in all conjunction analyses (Figs. 2-4; Table 4; Figure S5-6). In both FTD and

Table 1
Summary of studies included in the meta-analysis of atrophy patterns in FTD. [a]Age presented as mean ± standard deviation or range. bvFTD = behavioral variant frontotemporal dementia; SD = semantic dementia; PNFA = progressive nonfluent aphasia; HC = healthy controls; LTLV SD = left temporal lobar variant SD; RTLV right temporal lobar variant SD; TDP = TAR DNA binding Protein 43KD, FTLD-T = frontotemporal dementia with tau inclusions; FTLD-U = frontotemporal dementia with ubiquitin inclusions; FTD-A = Alzheimer pathology with frontotemporal dementia; CDR = clinical dementia rating scale; PiD = Pick's disease; IVS 10 + 16 = mutation in exon 10 + 16; IVS 10 + 3 = mutation in exon 10 + 3; N279K = N279K mutation; S305N = S305N mutation; P301L = P301L mutation; V337M = V337M mutation. More information on the studies is presented in Table S1 of the supplementary material.

Author	Participants (% female)	Age[a]	Diagnostic criteria
Agosta et al. 2009	bvFTD 31 (32%) HC 56 (58%)	58.4 ± 10.9 66.5 ± 9.4	Neary et al., 1998
Agosta et al. 2012	bvFTD 13 (31%) SD 7 (43%) PNFA 9 (67%) HC 25 (40%)	61.0 ± 7.5 71.5 ± 6.5 67.7 ± 5.1 64.2 ± 5.8	Neary et al., 1998
Ahmed et al. 2016	bvFTD 19 (47%) HC 25 (48%)	62 ± 8.3 66 ± 7.7	Rascovsky et al. 2011
Ahmed et al. 2019	bvFTD 28 (18%) HC 19 (32%)	60.9 ± 7.0 62.9 ± 6.9	Rascovsky et al. 2011
Ash et al. 2009	PNFA 6 SD 7 bvFTD 9 HC 31	70.7 ± 9.3 66.8 ± 7.3 64.8 ± 13.2 n.a.	Neary et al., 1998
Baez et al., 2016	bvFTD 26 (46%) HC 23 (43%)	66.1 ± 7.5 62.7 ± 9.0	Rascovsky et al. 2011
Baez et al., 2016	bvFTD 21 (48%) HC 19 (53%)	63.8 ± 7.3 60.4 ± 6.8	Rascovsky et al. 2011
Baez et al. 2019	bvFTD 16 (56%) HC 22 (68%)	65.8 ± 7.0 62.5 ± 7.1	Rascovsky et al. 2011
Bertoux et al. 2018	bvFTD 35 HC 29	67.2 ± 9.3 71.7 ± 5.8	Rascovsky et al. 2011
Boccardi et al. 2005	FTD 9 (22%) HC 26 (58%)	62.0 ± 5.0 69.0 ± 8.0	Neary et al., 1998
Boxer et al. 2003	SD 11 HC 15	66.2 ± 9.8 65.1 ± 8.3	Neary et al., 1998
Brambati et al. 2009	LTLV SD 13 (69%) RTLV SD 6 (50%) HC 25 (64%)	62.0 ± 6.3 62.5 ± 5.8 64.8 ± 6.9	Neary et al., 1998
Buhour et al. 2016	bvFTD 15 (67%) HC 15 (60%)	67.0 ± 8.2 66.5 ± 8.3	Rascovsky et al. 2011
Couto et al. 2013		69.8 ± 7.3	Rascovsky et al. 2011; Gorno-Tempini et al., 2011

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Table 1 (*continued*)

Author	Participants (% female)	Age[a]	Diagnostic criteria
	bvFTD 12 (42%) PNFA 10 (40%) HC 18 (33%)	64.9 ± 8.6 69.8 ± 7.3	
Desgranges et al. 2007	SD 10 HC 17	65.7 ± 8.6 65.8 ± 7.4	Neary et al., 1998
Flanagan et al. 2016	bvFTD 39 (33%) HC 61 (51%)	60.6 ± 7.5 63.6 ± 6.5	Rascovsky et al. 2011
Filippi et al. 2013	bvFTD 12 (67%) HC 30 (47%)	59.0 ± 8.0 59.0 ± 5.0	Rascovsky et al. 2011
García-Cordero et al. 2015	bvFTD 11 (55%) HC 14 (29%)	64.8 ± 5.0 57.2 ± 12.3	Rascovsky et al. 2011
Gorno-Tempini et al. 2004	PNFA 11 (73%) SD 10 (50%) HC 10 (50%)	67.9 ± 8.1 63.0 ± 5.8 69.1 ± 7.6	Neary et al., 1998
Gorno-Tempini et al. 2006	Mute PNFA 6 (83%) Nonmute PNFA 5 (100%) HC 40 (85%)	69.2 ± 8.2 62.4 ± 9.5 65.1	n.a.
Grossman et al. 2004	SD 8 PNFA 7 bvFTD 14 HC 12	65.5 ± 13.0 68.9 ± 11.4 63.1 ± 12.2 68.5 ± 9.4	Neary et al., 1998
Hardy et al. 2017	PNFA 10 (50%) SD 9 (33%) HC 19 (53%)	71.2 ± 8.9 63.8 ± 4.6 69.4 ± 4.5	Gorno-Tempini et al., 2011
Hornberger et al. 2011	bvFTD 14 (29%) HC 18 (50%)	59.3 ± 7.9 64.8 ± 5.3	Neary et al., 1998
Irish et al., 2016	SD 20 (40%) HC 35 (46%)	61.7 ± 4.8 64.4 ± 4.8	Gorno-Tempini et al., 2011
Irish et al., 2016	bvFTD 15 (40%) HC 20 (50%)	63.5 ± 7.4 67.1 ± 7.0	Rascovsky et al. 2011
Kanda et al. 2008	FTD 13 HC 20	64.9 65.2	Neary et al., 1998
Kim et al. 2007	FTLD-T 6 (17%) FTLD-U 8 (25%) HC 61 (57%)	67.7 ± 6.3 60.0 ± 10.0 68.0 ± 8.0	McKhann et al., 2001
Kipps et al. 2009	bvFTD 11 HC 12	62.1 ± 6.6 66.4 ± 4.9	Neary et al., 1998
Kumfor et al. 2018	bvFTD 19 (32%) SD 12 (50%) HC 20 (40%)	62.7 ± 8.7 64.9 ± 8.3 66.3 ± 6.1	Rascovsky et al. 2011; Gorno-Tempini et al., 2011
Lagarde et al. 2013	bvFTD 16 (38%) HC 18 (61%)	69.3 ± 10.0 67.8 ± 5.2	Rascovsky et al. 2011
Lagarde et al. 2015	bvFTD 18 (44%) HC 18 (61%)	69.7 ± 9.7 67.8 ± 5.2	Rascovsky et al. 2011
Lee et al. 2014	bvFTD 14 (29%) HC 14 (29%)	60.8 ± 6.9 62.2 ± 4.7	Rascovsky et al. 2011
Libon et al. 2009	bvFTD 51 SD 10 PFNA 11 HC 42	61.3 ± 10.6 66.1 ± 10.8 68.7 ± 8.1 n.a.	McKhann et al., 2001; The Lund and Manchester Groups 1994
Mandelli et al. 2016	bvFTD 23 (43%) PNFA 25 (44%) HC 34 (65%)	62.9 ± 6.5 66.6 ± 7.7 62.3 ± 6.6	Rascovsky et al. 2011; Gorno-Tempini et al., 2011
Melloni et al. 2016	bvFTD 26 (46%) HC 22 (73%)	68.0 ± 11.4 68.3 ± 5.8	Rascovsky et al. 2011
Mummery et al. 2000	SD 6 (17%) HC 14 (64%)	60.5 (58–65) 62.0 (60–65)	Neary et al., 1998
Pardini et al. 2009	FTD 22 (45%) HC 14	60.3 ± 8.3 n.a.	n.a.
Pereira et al. 2009	FTD-U 9 (44%) FTD-T 6 (17%) bvFTD 4 (25%) PNFA 3 (0%) SD 8 (50%) SD-U 5 (60%) SD-T 3 (33%) FTD-A 3 (33%) HC 25 (44%)	64.0 ± 5.7 61.8 ± 9.7 59.8 ± 7.5 68.3 ± 9.0 62.9 ± 6.4 65.8 ± 6.1 58.0 ± 3.6 65.3 ± 13.2 63.8 ± 7.2	Neary et al., 1998
Rabinovici et al. 2008	FTLD 18 (17%) HC 40 (58%)	62.5 ± 8.7 63.5 ± 5.8	McKhann et al., 2001
Rankin et al. 2011	bvFTD 5 (20%) HC 53 (55%)	n.a.	Cairns et al., 2007; Neary et al., 1998
Rosen et al. 2002	bvFTD 8 (25%) SD 12 (17%) HC 20 (20%)	61.8 (45–73) 67.8 (47–80) 65.4 (38–82)	Neary et al., 1998
			Neary et al., 1998

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Table 1 (*continued*)

Author	Participants (% female)	Age[a]	Diagnostic criteria
Seeley et al. 2008	bvFTD CDR(0,5) 15 (40%) bvFTD CDR(1) 15 (33%) bvFTD CDR (2–3) 15 (53%) HC 45 (49%)	65.9 ± 8.3 64.3 ± 8.9 62.3 ± 10.3 68.3 ± 7.9	
Shen et al. 2018	ALS-FTD 11 (27%) HC 20 (65%)	60.0 ± 12.7 55.3 ± 8.4	Neary et al., 1998
Whitwell et al. 2004	FTD-T 9 Tau negative FTD 8 HC 20	52.0 ± 8.7 62.0 ± 6.8 n.a.	Neary et al., 1998
Whitwell et al. 2005	FTD-U 9 (22%) PiD 7 (43%) Tau Exon 10 + 16 5 (40%) HC 20 (45%)	60.8 ± 2.8 51.6 ± 4.4 54.9 ± 2.2 55.7 ± 2.8	McKhann et al., 2001
Whitwell et al. 2009	IVS10 + 16 4 (25%) IVS10 + 3 3 (0%) N279K 3 (100%) S305N 2 (100%) P301L 4 (50%) V337M 3 (67%) HC 19 (42%)	56 (51–62) 46 (36–49) 49 (43–51) 33.5 (34–37) 52 (45–65) 56 (49–60) 53 (27–65)	Neary et al., 1998
Whitwell et al. 2011	bvFTD PiD 5 (40%) bvFTD TDP-1 5 (80%) HC 20 (50%)	64 (56–75) 68 (52–76) 63 (50–70)	Neary et al., 1998
S. M. Wilson et al. 2009	SD 5 (80%) HC 48 (79%)	61.4 ± 4.8 61.5 ± 10.3	Neary et al., 1998
S. M. Wilson et al. 2010	SD 25 (44%) PNFA 14 (93%) HC 10 (50%)	66.7 ± 6.0 67.8 ± 8.1 68.5 ± 5.9	Diagnostic guidelines developed by PPA researchers in Buenos Aires 2006 and Seattle 2009
N. A. Wilson et al. 2020	bvFTD 18 HC 22	n.a.	Rascovsky et al. 2011
Wong et al. 2016	bvFTD 22 (23%) HC 38 (50%)	61.0 ± 6.2 65.6 ± 5.5	Rascovsky et al. 2011
Zahn et al. 2005	PNFA 5 (20%) HC 10 (50%)	65.0 ± 7.4 65.8 ± 7.8	Rascovsky et al. 2011
Zamboni et al. 2008	FTD 62 (53%) HC 14 (50%)	61.2 ± 1.0 60.6 ± 1.7	Neary et al., 1998

social cognition the ventromedial prefrontal cortex, the left precentral gyrus and amygdalae were involved (Fig. 3; Table 4). All FTD subtypes showed overlap with both music perception and social cognition in the insulae. Whereas all FTD subtypes showed overlap with social cognition

Table 2
Summary of studies included in the meta-analysis of functional activity in music perception. [a]n = number of participants. [b]Age presented as mean ± standard deviation or range. More information on the studies is presented in Table S2 of the supplementary material.

Author Participants (% female)[a]	Age[b]	Experimental task	Control Task
Alluri et al. 2012 n = 11 (45%)	23.2 ± 3.7	Key clarity, increasing/decreasing pulse clarity, brightness, timbral complexity of a song ('adios nonino' by Astor Piazzolla)	
Altenmüller et al. 2014 n = 18 (50%)	28.7 ± 8.7	Participants listened to symphonic film music	Rest
Angulo-Perkins et al. 2014 n = 53 (45%)	28.0 ± 8.0	Participants listened to different musical pieces of piano, synthetic piano and violin	Non-vocal sounds and speech
Bangert et al. 2006 N = 14 (57%)	28.5 ± 7.3	Acoustic task which required passive listening to monophonic piano sequences	
Bianco et al. 2016 n = 29 (59%)	24.7 ± 2.9	Participants listened to piano pieces composed of 5 chords according to the rules of classical harmony with various melodic contours with either a congruent or incongruent ending	Rest
Bogert et al. 2016 n = 56 (61%)	28.2 ± 8.2	Participants listened to emotional musical fragments from movies	Rest
Brown and Martinez 2007 n = 11 (55%)	24.6 (19–46)	1. Passive listening to piano tones 2. Melody discrimination	1. Rest 2. Button-pressing control
Chapin et al. 2010 n = 14 (64%)	18–29	Participants listened to Chopin's Etude in E major, Op.10, No. 3 was performed by a skilled pianist	Mechanical performance task
Chen et al. 2012 n = 16 (50%)	27.1 (20–34)	Participants listened to melodies	
Escoffier et al. 2013 n = 16 (44%)	21.7 ± 1.9	Participants listened non-vocal musical excerpts from popular music genres	English sentences with swapped vowels
Flores-Gutiérrez et al. 2007 n = 6	25.0 ± 3.1	Participants listened to a passage of J. Prodromides, BWV 789 by J.S. Bach and G. Mahler's 5th symphony	
Groussard et al., 2010 n = 20 (50%)	24.6 ± 3.8	Participants listened to music in two parts, they then judged if these two match or are different pieces. They also judged the familiarity of musical pieces.	Sentences and familiarity of popular expressions.
Groussard et al., 2010 n = 40 (50%)	20–35	Participants judged the familiarity of musical pieces	
Habermeyer et al. 2009 n = 16 (13%)	44.5 ± 9.9 (n = 8) 42.9 ± 10.7 (n = 8)	Participants listened to standard and deviant melodies	

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Table 2 (*continued*)

Author Participants (% female)[a]	Age[b]	Experimental task	Control Task
Janata 2009 n = 13 (85%)	20.0 (18–22)	Participants listened to music of the top 100 pop and R&B charts from when they were between 7 and 19 years of age	
Janata et al., 2002 n = 12 (58%)	28.5 (20–41)	Participants listened to different classical music parts or had to attend different elements of the music	Rest
Janata et al., 2002 n = 8 (50%)	26.0 ± 8.9	Participants listened to a melody that modulated through all 24 minor and major keys and performed tonality and timbre tasks	
Langheim et al. 2002 n = 6 (67%)	27.0 (22–32)	Participants listened to music	Rest
Levitin and Menon 2003 n = 13 (54%)	19.4–23.6	Participants listened to classical music	'Scrambled music'; quasi musical stimulus
Mitterschiffthaler et al. 2007 n = 16 (50%)	29.5 ± 5.5	Participants listened to music that was either rated as happy, sad or neutral	
Morrison et al. 2003 n = 12 (67%)	36.3	Participants (6 musicians and 6 non-musicians) listened to Western and Chinese music	Rest
Musso et al. 2015 n = 11 (55%)	24.3 (18–35)	Participants listened to chord sequences based on classical and deviant idioms	Spoken sentences which were either baseline stimuli or deviant stimuli
Park et al. 2014 n = 24 (58%)	19.0 ± 0.6 (n = 12) 20.3 ± 1.8 (n = 12)	Participants listened to music pieces with different emotions	Rest
Rogalsky et al. 2011 n = 20 (55%)	22.6 (18–31)	Participants listened to piano pieces	1. Rest 2. Meaningless sentences
Sachs et al. 2020 n = 40 (53%)	24.1 ± 6.2	Participants listened to sad music	
Schmithorst 2005 n = 15 (27%)	37.8 ± 15.2	Participants listened to famous melodies	
Toiviainen et al. 2014 n = 15 (33%)	25.7 ± 5.2	Participants listened to the B-side of Abbey Road by the Beatles	
Trost et al. 2012 n = 15 (47%)	28.8 ± 9.9	Participants listened to different types of classical music from the last 4 centuries	Atonal random melodies

in striatal, basal forebrain and mesolimbic regions, only bvFTD showed overlap in these regions with music perception (Figure S7-10; Table S12-13). Subgroup analysis on empathy studies showed overlap with FTD in the insulae, the midcingulate gyrus, amygdalae, striatal regions and left precentral gyrus (Figure S11-12; Table S14). Theory of Mind and FTD showed overlap in the ventromedial prefrontal cortex, temporal poles, left inferior frontal gyri connecting the left striatum (Figure S11; Table S15).

4. Discussion

In this meta-analysis we demonstrated a close neuroanatomical overlap of music perception and social cognition processing with the FTD atrophy profile.

Table 3
Summary of studies included in the meta-analysis of functional activity in social cognition. [a]n = number of participants. [b]Age presented as mean ± standard deviation or range. More information on the studies is presented in Table S3 of the supplementary material. For more information on the studies see Table S3.

Author Participants (% female)[a]	Age[b]	Experimental task	Control task
Abraham et al. 2008 n = 17 (53%)	25.7 (22–30)	Intentional (mentalizing) relations between persons	Non-intentional relational between objects or persons
Abraham et al. 2010 n = 22 (50%)	26.1 (21–35)	Participants made judgments on intentional states based on scenarios (beliefs, desires)	Non-mental state control question
Adams et al. 2010 n = 28 (64%)	18–27	Reading the mind in the eyes task (Baron-Cohen et al. 2001)	Gender discrimination task (Baron-Cohen et al. 1999)
Aichhorn et al. 2006 n = 18 (56%)	28.5 (21–55)	Judgments about positions of objects from third person perspective	Judgments about positions of objects from first person perspective
Aichhorn et al. 2009 n = 21 (38%)	24 (21–41)	False belief stories	False photograph stories
Akitsuki and Decety 2009 n = 26 (54%)	24.4 ± 5.8	Participants watched painful stimuli	Non-painful stimuli
Assaf et al. 2009 n = 19 (47%)	32.3 ± 10.4	Participants play a game where mentalizing is needed	A choice in the game where no mentalizing is needed
Azevedo et al. 2013 n = 27 (59%)	23.9	Participants watched painful stimuli	Non-painful stimuli
Azevedo et al. 2014 n = 12 (100%)	22.2 ± 2.6	Participants watched painful stimuli	Non-painful stimuli
Bahnemann et al. 2009 n = 25 (12%)	26 ± 4.4	Judgment of mental states from a movie (Dziobek et al. 2006)	Participants make appearance judgments in the movie (Baron-Cohen et al. 1999)
Benuzzi et al. 2008 n = 15 (100%)	23.5 (19–31)	Participants watched painful stimuli	Non-painful stimuli
Benuzzi et al. 2018 n = 27 (100%)	21.3 ± 1.6	Participants watched painful facial expressions	Neutral facial expressions
Berlingeri et al. 2016 n = 25 (52%)	25.3 ± 4.8	Participants judged painful experience of a character	Non-painful stimuli
Boccadoro et al. 2019 n = 68 (75%)	31.1 ± 10.5	Participants watched false belief videos to activate spontaneous ToM	True belief videos
Bodden et al. 2013 n = 30 (50%)	25.3 ± 2.5	Judgment about the affective and cognitive ToM aspects of a scenario	Participants answered questions about the physical state of a scenario
Bos et al. 2015 n = 24 (0%)	23.1 (19–27)	Participants watched painful stimuli	Non-painful stimuli
Botvinick et al. 2005 n = 12 (100%)	20–30	Participants watched painful facial expressions	Neutral facial expressions
Brüne et al. 2008 n = 13 (70%)	26.5 ± 5.3	Participants judged intentions and expectations of the protagonist in a cartoon	Participants properties of objects in the cartoon
Bruneau et al. 2012 n = 14 (57%)	23.5 ± 4.1	Participants read stories about painful physical and emotional scenarios	Non painful physical and emotional scenarios

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Table 3 (*continued*)

Author Participants (% female)[a]	Age[b]	Experimental task	Control task
Bruneau et al. 2015 n = 18 (78%)	22.2 ± 3.6	Participants actively emphasized in emotional painful scenarios	Participants stayed objective
Brunnlieb et al. 2013 n = 18 (0%)	19–37	Participants watched pictures of an emotionally charged situation (Krämer et al. 2010)	Pictures of neutral situations
Budell et al. 2010 n = 18 (50%)	18–25	Participants judged the amount of pain in painful facial expressions	Neutral facial expressions
Canessa et al. 2012 n = 27 (52%)	26.3 ± 4.2	Participants viewed images displaying affective social interactions	Images displaying natural or urban landscapes
Cassidy et al. 2020 n = 75 (63%)	21.6 ± 2.8 (n = 40) 71.7 ± 6.1 (n = 35)	False belief stories (Saxe and Kanwisher 2003)	False photographs
Castelli et al. 2010 n = 24 (75%)	25.2 ± 3.5 (n = 12) 65.2 ± 5.7 (n = 12)	Reading the mind in the eyes task (Baron-Cohen et al. 2001)	Gender discrimination task (Baron-Cohen et al. 1999)
Chaminade et al. 2012 n = 19 (0%)	21.5 ± 4.9	A competitive game was played against a fellow human	A computer playing randomly
Cheng et al. 2007 n = 14 (50%)	n.a.	Participants watched painful stimuli	Non-painful stimuli
Cheng et al. 2010 n = 36 (50%)	23 ± 3	Participants watched painful stimuli	Non-painful stimuli
Cheon et al. 2013 n = 27 (44%)	23.1 ± 4.4 (n = 13) 25.1 ± 4.8 (n = 14)	Participants watched pictures of emotionally painful scenarios	Non-painful scenarios
Cheung et al. 2012 n = 23	23.5 ± 1.1	Cartoon false belief stories	Non-mentalistic pictures and verbal stories (fillers)
Chiao et al. 2009 n = 14 (100%)	22.9 ± 3.7	Participants watched pictures of emotionally painful scenarios	Non-painful scenarios
Christov-Moore and Iacoboni 2019 n = 70 (51%)	18–35	Participants watched painful stimuli	Non-painful stimuli
Contreras et al. 2013 n = 14 (43%)	19.9 (18–23)	False belief stories (Saxe and Kanwisher 2003)	False photographs
Corradi-Dell'Acqua et al. 2011 n = 28 (100%)	19–31	Participants watched painful noxious stimuli	Non-painful/noxious stimuli
Corradi-Dell'Acqua et al. 2014 n = 46 (100%)	18–31	Judgment about a protagonists beliefs, emotions and pain (Saxe and Kanwisher 2003)	Stories without a protagonist, but with physical representation on a map or photograph
Danziger et al. 2009 n = 13 (54%)	33 ± 9.0	Participants watched painful stimuli and facial expressions	Non-painful stimuli and neutral expressions
de Achával et al. 2012 n = 14 (43%)	28.4 ± 8.3	Reading the mind in the eyes task (S Baron-Cohen et al. 2001)	Gender discrimination task (Baron-Cohen et al. 1999)
de Greck et al., 2012 n = 20 (60%)	37.0 ± 10.6	Participants actively emphasized with characters	Smoothed pictures
Greck et al., 2012 n = 20 (55%)	23 (21–26)	Participants actively emphasized with characters	Skin color evaluation
	27.0 ± 5.0		Neutral expressions
Deeley et al. 2006 n = 9 (0%)		Participants watched fearful facial expressions	
Derntl et al. 2010 n = 24 (50%)	28.3 ± 6.6 (n = 12) 26.3 ± 4.1 (n = 12)	1. Participants judged emotions from faces 2. Emotional perspective taking task (ToM) 3. Affective responsiveness task (empathy)	1. Gender discrimination task 2. Characteristics task 3. Sentence forming task
Deuse et al. 2016 n = 38 (53%)	24.1 (18–30)	Mental state judgments were made about daily life situations as pleasant or unpleasant on a 9-point scale	Comparable scenes to the experimental task but without people
Dodell-Feder et al. 2011 n = 62 (65%)	22.0 ± 3.2	False belief stories (Saxe and Kanwisher 2003)	False photographs and maps
Döhnel et al. 2012 n = 18 (44%)	24.7 ± 2.2	False belief story ''Sally Anne paradigm'' (Baron-Cohen et al. 1985)	Non-mental control questions
Döhnel et al. 2017 n = 22 (55%)	25.3 ± 4.6	Emotional and behavioral ''Sally Anne paradigm'' (Baron-Cohen et al. 1985)	True belief stories
Dufour et al. 2013 n = 462 (52%)	24.9 (18–69)	False belief stories	False photographs
Dungan and Young 2019 n = 26 (52%)	23.7 ± 4.4	Participants judged mental states (why)	Participants judged behavior (how)
Enzi et al. 2016 n = 20 (0%)	27.0 ± 5.1	Participants watched painful stimuli	Non-painful stimuli
Ernst et al. 2013 n = 18 (67%)	27.0 ± 7.6	Participants judged the empathic ability to faces	Smoothed photographs
Fan et al. 2014 n = 21 (0%)	19.3 ± 3.4	Participants watched painful stimuli	Non-painful stimuli
Frank et al. 2015 n = 34 (50%)	28 ± 0.42 (n = 17) 29 ± 0.5 (n = 17)	False belief stories	Unlinked sentences
Feng et al. 2016 n = 22 (50%)	22.2 ± 1.9	Participants watched painful stimuli	Non-painful stimuli
Fourie et al. 2017 n = 38 (55%)	40.1 ± 4.1 (n = 19) 41.5 ± 5.8 (n = 19)	Participants watched facial expressions of people in physical pain and scenarios of social pain	Neutral expressions and scenarios
Fujino et al. 2014 n = 11 (82%)	32.3 ± 10.5	Participants watched painful stimuli	Non-painful stimuli
Gallagher et al. 2000 n = 6 (17%)	30.0 (23–36)	False belief stories (Fletcher et al. 1995)	Participants judged why something physical happened in a non-ToM story
Gallagher and Frith 2004 n = 12 (42%)	36.0 (28.4–59.5)	Participants judged expression of inner states by gestures	Neutral gestures
Geiger et al. 2019 n = 32 (47%)	25.8 ± 4.9	Participants judged emotional states from animations	Judgment of activities
Gilbert et al. 2007 n = 16 (56%)	21 (18–27)	Participants judged if the experimenter was trying to be helpful in a task of time	Participants are told a computer manages time randomly
Gobbini et al. 2007 n = 12 (58%)	22.0 ± 2.0	False belief stories (Fletcher et al. 1995)	Questions about stories describing human activity

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Table 3 (*continued*)

Author Participants (% female)[a]	Age[b]	Experimental task	Control task
			without mental state attribution
Göttlich et al. 2017 n = 44 (75%)	27.8 ± 4.8 (n = 17) 23.0 ± 3.3 (n = 27)	Participants viewed socio-affective scenarios to elicit emphatic responses	Neutral scenarios
Grèzes et al. 2007 n = 16 (63%)	25	Participants watched fearful body expressions	Neutral body expressions
Grice-Jackson et al. 2017 n = 44 (59%)	24.0 ± 1.4	Participants judged whether they experienced pain while watching painful stimuli	Non-painful stimuli
Gu and Han 2007 n = 12 (42%)	21.0 ± 1.2	Participants watched painful stimuli	Non-painful stimuli
Gu et al. 2010 n = 18 (50%)	24.8 (22–28)	Participants made pain judgments from painful stimuli	Non-painful stimuli
Gu et al. 2013 n = 18 (50%)	25.2 (22–34)	Participants made pain judgments from painful stimuli	Non-painful stimuli
Guo et al. 2013 n = 40 (75%)	22.2 ± 2.7	Participants watched painful stimuli	Non-painful stimuli
Gweon et al. 2012 n = 8 (75%)	21.5 (18–25)	Stories about a protagonists mental state	Stories about physical events
Haas et al. 2015 n = 16 (56%)	21.8 ± 2.1	An emotion attribution task judging the cause of an emotional response	Gender match task
Hadjikhani et al. 2014 n = 31 (10%)	22.5 ± 7.5	Participants watched painful facial expressions	Non-painful stimuli
Han et al. 2009 n = 46 (50%)	21.0 ± 1.6 (n = 24) 22.6 ± 2.3 (n = 22)	Participants watched painful stimuli with or without painful expressions	Non-painful stimuli and neutral expressions
Han et al. 2017) n = 33 (48%)	22.9	Participants watched painful stimuli	Non-painful stimuli
Harris et al. 2005 n = 12 (92%)	20	Participants judged behavior to the characteristics of a person	Baseline condition
Hervé et al. 2013 n = 42 (38%)	30.9 ± 8.6	Participants judged the mental state of a character	Participants judged if a sentence was true or not
Hooker et al. 2008 n = 20 (55%)	21.0 (19–26)	False belief stories (Fletcher et al. 1995)	True belief stories
Hooker et al. 2010 n = 15 (47%)	21 (18–25)	Participants viewed a scenario with change in beliefs and mental states	No change in beliefs and mental states
Jackson et al. 2005 n = 15 (47%)	22 ± 2.6	Participants watched painful stimuli	Non-painful stimuli
Jackson et al. 2006 n = 34 (59%)	29 ± 6.5	Participants watched painful stimuli	Non-painful stimuli
Jacoby et al. 2016 n = 20 (60%)	25.3 (18–39)	1. False belief task (ToM; Dodell-Feder et al. 2011) 2. Stories about painful physical and emotional scenarios (empathy; Bruneau et al. 2012)	1. False photographs or maps 2. Non-painful physical and emotional scenarios
Jankowiak-Siuda et al. 2015 n = 27 (52%)	25–35	Participants watched painful stimuli	Non-painful stimuli

Table 3 (*continued*)

Author Participants (% female)[a]	Age[b]	Experimental task	Control task
Jenkins and Mitchell 2010 n = 15 (60%)	19.8 (18–22)	Participants judged mental states in an (un) ambiguous scenario	Nonsocial physical representations (e.g. photographs)
Jimura et al. 2010 n = 34 (47%)	20–28	False belief stories (Saxe and Kanwisher 2003)	Participants judged physical aspects of the story
Kaiser et al. 2008 n = 24 (50%)	28.7 ± 6.6 (n = 12) 27.6 ± 4.9 (n = 12)	Participants judged a characters visual perspective	Own perspective
Kana et al. 2009 n = 12 (0%)	24.4 ± 3.7	Mental states attribution to movement of geometrical figures (Castelli et al. 2002)	Random movements
Kana et al. 2016 n = 15	24.0 ± 13.5	Participants judged emotional facial/ body expressions	Neutral expressions
Kana and Travers 2012 n = 26 (54%)	21.0 (18.5–35.8)	Participants judged emotional body expressions	Participants judged actions
Kandylaki et al. 2015 n = 20	24.3 ± 2.1	Participants listened to stories with false belief passages and judged beliefs	Judgments about physical events in the story.
Kanske et al. 2015 n = 178 (60%)	40.9 ± 9.5	1. False belief task (ToM; Dodell-Feder et al. 2011) 2. Socio-affective video task (empathy; Klimecki et al. 2013)	1. nonToM story contents 2. Neutral videos
Kim et al. 2005 n = 14 (50%)	23.3 ± 2.0	Participant judged if the facial affect was appropriate for a situation	Participant were asked whether the gender of two subjects was the same
Kim et al. 2007 n = 21 (48%)	25.4 ± 2.6	Participants imagined facial affective expression of emotional faces	Imagery of neutral faces
Kim et al. 2009 n = 14 (43%)	27.5 ± 3.3	Participants made judgments on causality of facial expressions	Clear information on causality
Kircher et al. 2009 n = 14 (0%)	27.4	Participants played a mentalizing game	Non-mentalizing game
Kobayashi et al. 2008 n = 16 (50%)	29.7 ± 4.6	False belief stories	Baseline condition
Kockler et al. 2010 n = 18 (0%)	24.4 ± 2.1	Participants judged a characters visual perspective	Own perspective
Koelkebeck et al. 2011 n = 15 (53%)	30.9 ± 8.1	Judgment of 'moving shapes' paradigm with interacting triangles (Abell et al. 2000)	Random movements
Krach et al. 2008 n = 20 (0%)	24.5 ± 3.0	Participants played a mentalizing game ('Prisoners dilemma game)	Control condition
Krach et al. 2009 n = 24 (50%)	27.4 (19–40)	Participants played a mentalizing game ('Prisoners dilemma game)	Baseline game
Krach et al. 2011 n = 32 (53%)	22.8 ± 2.2	Participants watched vicarious embarrassing social situations	Neutral situations
Krach et al. 2015 n = 16 (0%)	24.3 ± 2.9	Participants watched vicarious embarrassing social	Neutral situations and non-painful stimuli

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Table 3 (*continued*)

Author Participants (% female)[a]	Age[b]	Experimental task	Control task
		situations and painful stimuli	
Krämer et al. 2010 n = 16 (63%)	27.8 ± 4.8	Participants were showed pictures of an emotionally charged situation	Pictures of neutral situations
Lamm and Decety 2008 n = 18 (50%)	23.7 ± 4.0	Participants watched painful stimuli	Non-painful stimuli
Lancaster et al. 2015) n = 37 (0%)	23.7 (18–29)	Social attribution task (Schultz et al. 2003)	Random movements
Lavoie et al. 2016 n = 19 (16%)	28.8 ± 7.9	Participants judged a characters feelings or thoughts	Participants answered questions about physical events in a scenario
Lawrence et al. 2006 n = 12 (50%)	32.2 ± 9.9	Participants performed emotion perception tasks	Physical properties
Lee et al. 2010 n = 18 (50%)	25.8 ± 2.2	Participants judged comics on various types of empathic causality	Physical causality
Lee et al. 2013 n = 12 (100%)	72.3 ± 6.2	Participants watched emotional facial expressions	Neutral expressions
Leiberg et al. 2012 n = 24 (100%)	24.1 (18–33)	Participants viewed emotional scenarios	Neutral scenarios
Leitman et al. 2010 n = 20 (0%)	28 ± 5	Participants judged emotional prosody from voices	Neutral prosody judgment
Lewis et al. 2017 n = 17 (53%)	22 ± 2.9	Participants answered true/false mentalizing questions	Factual memory processing
Liew et al. 2011 n = 18 (44%)	23 ± 2.3	Participants judged intentions of actors using gestures	Still photo of the actor
Lin et al. 2018 n = 39 (46%)	22.2 ± 2.7	False belief task (Dodell-Feder et al. 2011)	False photo task
Lombardo et al. 2010 n = 33 (0%)	28.0 ± 6.1	Participants answered questions about others mental states	Participants answered questions about physical characteristics
Lotze et al. 2006 n = 20 (50%)	52.3 ± 12.4	Participants viewed emotional/expressive gestures	Isolated hand movements
Luo et al. 2014 n = 36 (50%)	21.3	Participants watched painful stimuli	Non-painful stimuli
Malhi et al. 2008 n = 20 (45%)	35.8 ± 10.4	Observing geometric shapes interacting (Castelli et al. 2000)	Random movements
Mano et al. 2009 n = 18 (56%)	25.2 ± 2.5	Participants judged emotions and beliefs in a scenario	Unrelated stories
Marjoram et al. 2006 n = 13 (38%)	29.6 ± 1.6	Participants viewed jokes needing ToM for understanding (Gallagher et al. 2000)	Physical jokes
Martin and Weisberg 2003 n = 12 (50%)	27.5 (23–34)	Geometric shapes conveying social interactions	Mechanical actions
Mathur et al. 2010 n = 28 (46%)	23.8 ± 0.8	Participants watched people in emotionally painful situations	Neutral situations
Mathur et al. 2016 n = 15 (53%)	25.3 ± 4.7	Participants watched people, animals and nature in emotionally painful situations	Neutral situations
Mazza et al. 2013 n = 10 (100%)	24.4 ± 4.4	Participants judged pictures with negative emotional valence	Neutral pictures
Mazzola et al. 2010 n = 30 (37%)	36.8	Participants watched painful facial expressions	Neutral facial expressions
McAdams and Krawczyk 2011 n = 17 (100%)	24.7 ± 6.6	Participants judged how shapes interacted	Visuospatial task
Meaux and Vuilleumier 2016 n = 26 (50%)	25.9 ± 5.5	Participants judged facial emotions (happy/angry)	Neutral emotions
Melchers et al. 2015 n = 60 (65%)	29.5 ± 5.4	Participants watched vicarious embarrassing social situations	Neutral situations
Mercadillo et al. 2011 n = 24 (50%)	27.0 ± 2.5	Participants watched social scenarios of people suffering	Neutral social scenarios
Meyer et al. 2015 n = 25 (60%)	21.6 ± 2.5	Participants made personality trait judgments about friends	Participants alphabetized the names
Mier et al., 2010 n = 40 (50%)	25.3 ± 3.5	Participants made emotion recognition and mentalizing judgments from faces	Judgment of physical features
Mier et al., 2010 n = 16 (31%)	37.0 ± 8.2	Participants made emotion recognition and mentalizing judgments from faces	Judgment of physical features
Mitchell 2008 n = 20 (55%)	23 (19–29)	False belief stories (Saxe and Kanwisher 2003)	False photograph stories
Moessnang et al. 2017 n = 28 (50%)	22.9 ± 2.8	Judgment of 'moving shapes' paradigm with interacting triangles (Abell et al. 2000)	Goal directed movements
Moll et al. 2007 n = 12 (50%)	28.5 ± 9.6	Participants read scenarios that evoked empathetic/ compassionate feelings	Neutral scenarios
Moran et al. 2012 n = 48 (44%)	23.0 ± 0.9 (n = 31) 71.8 ± 1.9 (n = 17)	Animate movement task, moral judgment task (Young et al. 2007) and False belief stories (Saxe and Kanwisher 2003)	Mechanical movies, neutral outcome and false photo stories
Morelli et al. 2014 n = 32 (50%)	19.9 ± 1.4	Participants empathized with people in photo's of emotional scenarios	Neutral images
Moriguchi et al. 2007 n = 14 (86%)	20.8 ± 0.9	Participants watched painful stimuli (Jackson et al. 2005)	Non-painful stimuli
Morrison et al. 2004 n = 14 (64%)	23.0	Participants watched painful stimuli	Non-painful stimuli
Morrison and Downing 2007 n = 12 (42%)	31.0	Participants watched painful stimuli	Non-painful stimuli
Morrison et al. 2007 n = 16 (50%)	27.0	Participants watched painful stimuli	Non-painful stimuli
Morrison et al. 2013 n = 14 (50%)	23–35	Participants watched painful stimuli	Non-painful stimuli
Murphy et al. 2010 n = 10 (60%)	29.6 ± 8.4	Participants judged personality attributes	Semantic positivity evaluation of adjectives
Narumoto et al. 2000 n = 8 (38%)	23–29	Facial emotion recognition task	Gender matching task

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Table 3 (*continued*)

Author Participants (% female)[a]	Age[b]	Experimental task	Control task
Nomi et al. 2008 n = 14 (50%)	28.6 ± 5.5	Participants recognized and shared emotions of presented facial expressions	Count earrings
Nummenmaa et al. 2008 n = 10 (100%)	26 ± 5.6	Participants empathized with emotional scenes	Neutral scenes
Ochsner et al. 2004 n = 13 (54%) 7	29.5	Participants judged whether a character felt pleasant, unpleasant or neutral	Participants judged whether a photo was taken outside or inside
Otti et al. 2015 n = 20 (65%)	45.6 ± 14.0	Participants judged a scenario where triangles were coaxing, mocking, seducing and surprising each other	Participants judged a scenario where triangles were moving or rotating without any interaction
Özdem et al. 2017 n = 20	18–26	False belief stories (Saxe and Kanwisher 2003)	False photograph stories
Paulus et al. 2018 n = 17 (0%)	24.1 ± 3.0	Participants emphasized with characters in embarrassing scenarios	Neutral scenarios
Pichon et al. 2008 n = 16 (44%)	18–26	Participants judged emotions from angry whole body expression	Neutral body expressions
Platek et al. 2004 n = 5	n.a.	Reading the mind in the eyes task (Baron-Cohen et al. 2001)	Participants viewed a crosshair
Powell et al. 2017 n = 12 (0%)	36.4 ± 13.9	Intentional judgments and mental state attributions (ToM & empathy; Brunet et al. 2000)	Physical causality
Preis et al. 2013 n = 64 (50%)	22.9	Participants watched painful stimuli	Non-painful stimuli
Prochnow et al. 2013 n = 15 (47%)	22.3 ± 1.4	Participants watched and judged emotional faces and gestures	Scrambled stimuli
Prochnow et al. 2014 n = 26 (47%)	38.3 ± 12.0	Participants matched facial expressions with situations	Scrambled images with unrelated sentences
Qiao-Tasserit et al. 2018 n = 24 (54%)	27.6 ± 6.0	Participants watched painful stimuli	Non-painful stimuli
Rabin et al. 2010 n = 18 (50%)	57.2 ± 8.0	Participants viewed photo's and judged mental state attributions vividly	Scenarios lacking details
Rapp et al. 2010 n = 15 (100%)	28.1 ± 8.0	Participants judged irony of sentences	Literal target sentences
Regenbogen et al. 2012 n = 27 (48%)	34.1 ± 9.8	Participants judged valence from emotional prosody, facial expressions and speech content	Neutral content
Reniers et al. 2014 n = 15 (0%)	18–40	Imagining what someone feels (empathy) and would make them feel better (ToM)	Neutral contexts
Rilling et al. 2008 n = 20 (100%)	20.8 ± 1.6	Participants played a mentalizing game ('Prisoners dilemma game)	Gamble game
Rosenblau et al. 2016 n = 22 (27%)	31.3 ± 8.5	Participants judged changes in affective states of a protagonist in a video	Physical inference tasks
Roser et al. 2012 n = 14 (0%)	27.3 ± 3.5	Participants judged intentions and beliefs in cartoons (Brüne 2005)	Participants judged properties of objects displayed
Rothmayr et al. 2011 n = 12 (58%)	23.7 (23–24)	False belief story ''Sally Anne paradigm'' (Baron-Cohen et al. 1985).	True belief story
Ruckmann et al. 2015 n = 30 (50%)	24.5 ± 3.7	Participants watched painful stimuli	Non-painful stimuli
Saft et al. 2013 n = 26 (27%)	28.8 ± 4.1	Participants judged intentions and beliefs in cartoons (Martin Brüne 2005)	Participants judged properties of objects displayed
Samson et al. 2008 n = 17 (53%)	26.1 ± 3.3	Participants viewed comic cartoons that required ToM for understanding	Non-ToM cartoons
Saxe and Powell 2006 n = 12 (75%)	19–26	1. False belief stories 2. 'Thought stories' where participants judged protagonist's beliefs and thoughts	1. False-photograph stories 2. A story of the protagonist's physical, social characteristics and physical feelings
Schlaffke et al. 2015 n = 39 (0%)	25.9 ± 5.8	Participants judged a characters feelings (affective ToM) and beliefs (cognitive ToM)	Non-mentalizing questions about the stories
Schmitgen et al. 2016 n = 21 (9%)	23.7 ± 3.1	Participants judged a protagonist's mental state as worse, equal or better after an event	Participants judged the number of living beings in a scene
Schnell et al. 2011 n = 21 (43%)	25.5 ± 5.0	Participants viewed cartoons, which they judged affective and visuospatial states	Participants answered questions about their own affective and visuospatial states
Schulte-Rüther et al. 2008 n = 26 (54%)	24.8 ± 3.7	Emotion recognition and affect task from facial expressions	Age/gender task
Schuwerk et al. 2017 n = 24 (50%)	22.8 ± 3.0	Participants belief was they received cues from a person	Participants belief was they received cues from the computer
Seara-Cardoso et al. 2015 n = 46 (0%)	27.9 (19–40)	Participants watched painful stimuli	Non-painful stimuli
Seara-Cardoso et al. 2016 n = 30 (0%)	26.9 (20–40)	Participants judged their own affective state watching facial expressions	Fixation cross
Seger et al. 2004 n = 12 (67%)	23.6 (20–32)	Participants made judgments if someone would like particular food	Judgments about the number of vowels
Sheng et al. 2014 n = 21 (52%)	22.0 ± 1.8	Participants judged painful facial expressions	Neutral facial expressions
Shibata et al. 2010 n = 13 (23%)	23.8 (20–29)	Participants judged irony of sentences	Literal sentences
Shibata et al. 2011 n = 15 (27%)	25.2	Participants judged the meaning of indirect sentences	Literal sentences
Simon et al. 2006 n = 17 (53%)	23.1 ± 4.1	Participants judged gender on painful facial expressions	Neutral facial expressions
	25.8 ± 6.9		Non-painful stimuli

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Table 3 (*continued*)

Author Participants (% female)[a]	Age[b]	Experimental task	Control task
Singer et al. 2004 n = 16 (100%)		Participants watched painful stimuli	
Sommer et al. 2007 n = 16 (50%)	26.0 (23–37)	False belief story ''Sally Anne paradigm'' (Simon Baron-Cohen et al. 1985)	True belief story
Specht and Wigglesworth 2018 n = 18 (0%)	25.7 ± 2.5	Participants judged intentions of a character (Brunet et al. 2000)	Participants judged which cartoon was displayed twice
Spiers and Maguire 2006 n = 20 (0%)	49.8 ± 8.5	Mental state attributions during a game	Coasting condition
Spotorno et al. 2012 n = 20 (60%)	22	Participants judged irony of sentences	Literal sentences
Sprengelmeyer et al. 1998 n = 6 (67%)	23.5 ± 1.3	Participants judged gender on emotional facial expressions	Neutral facial expressions
Spunt et al. 2011 n = 15 (60%)	19.5 ± 1.9	Participants judged the motive of a character ('why')	Participants judged what a character was doing
Spunt and Ralph Adolphs, 2014 n = 29 (34%)	27.1 (19–38)	1. False belief stories (Dodell-Feder et al. 2011; Saxe and Kanwisher 2003) 2. Participants judged motive	1. False photograph stories 2. Participants judged physical events
Spunt and Lieberman 2012 n = 22 (55%)	21.6 (19–32)	Participants judged the motive of a character ('why')	Participants judged what a character was doing
Spunt et al. 2017 n = 16 (50%)	29.0 (21–46)	Participants judged an emotion from a human, dog or monkey	Participants judged characteristics of facial expressions
Sripada et al. 2009 n = 26 (62%)	28.0 ± 8.2	Participants played the 'trust game' against a human	Participants played against a computer
Suzuki et al. 2012 n = 26	20–35	Participants predicted the choices of another person	Random rewards
Takahashi et al. 2015 n = 38 (100%)	22.1 ± 4.7	Participants judged the intensity of sadness of faces with tears	Participants judged the intensity of sadness of faces without tears
Tamm et al. 2017 n = 86 (51%)	23.0 (n = 47) 68.0 (n = 39)	Participants watched painful stimuli and rated their own unpleasant affect	Non-painful stimuli
Tholen et al. 2020 n = 130 (55%)	40.4 ± 9.0	1. False belief task (ToM; Dodell-Feder et al. 2011) 2. Socio-affective video task (empathy; Klimecki et al. 2013)	1. nonToM story contents 2. Neutral videos
Thye et al. 2018 18 = (72%)	20.2 ± 1.4	1. Reading the mind in the eyes (S Baron-Cohen et al. 2001) 2. Reading the mind in the voice (Rutherford, 2002) 3. Intentional judgments (Brunet et al. 2000)	1. Gender discrimination task 2. Gender discrimination task 3. Physical events
Todorov et al. 2007 n = 11 (27%)	21 (18–32)	Participants judged faces based on their personality traits	Novel faces
Uchiyama et al. 2006 n = 20 (50%)	21.9 ± 2.7	Participants judged if a sentence expressed sarcasm	Literal sentences
	27.3		Static right hand
Ushida et al. 2008 n = 15 (53%)		Participants watched painful stimuli	
Vachon-Presseau et al. 2012 n = 20 (50%)	36 ± 10	Participants watched painful stimuli and painful facial expressions	Neutral stimuli
van Ackeren et al. 2016 n = 25 (100%)	18–35	Participants judged if a sentence expressed indirect replies and requests	Direct replies
van der Meer et al. 2011 n = 19 (47%)	21.6 ± 2.6	False belief stories	Physical events in a scenario
Van Hoeck et al. 2014 n = 19	19–29	False belief stories	True belief
Vanderwal et al. 2008 n = 17 (41%)	21.5 ± 1.8	Social attribution task (Schultz et al. 2003)	Bumper cars condition
Veroude et al. 2012 n = 25 (100%)	19.1 (18.1–19.9)	Participants made mental state judgments	Baseline condition
Vistoli et al. 2016 n = 21 (14%)	29.2 ± 7.9	Participants watched painful stimuli	Non-painful stimuli
Vogeley et al. 2001 n = 8 (0%)	25–36	Participants judged the mental state of a character (Fletcher et al. 1995)	Sentences with no semantic consistency or coherence
Völlm et al. 2006 n = 13 (0%)	24.9 (19–36)	Intentional judgments (Brunet et al. 2000) and empathic judgment	Physical causality
Walter et al. 2004 n = 13 (54%)	25.2 ± 2.0	Participants judged communicative intentions in stories	Physical causality
Walter et al. 2009 n = 12 (50%)	24.8 ± 2.6	Participants judged private and social intentions in stories	Physical causality
Wang et al. 2006 n = 12 (50%)	26.9 ± 3.5	Participants judged irony of sentences	Literal sentences
Wang et al. 2015 n = 56 (45%)	19.3 ± 0.9	Participants performed ToM and empathy tasks (Völlm et al. 2006)	Physical causality
Whitehead and Armony 2019 n = 30 (50%)	24.0 ± 2.6	Participants judged expressions of fear from faces, bodies, prosody and vocalization	Neutral expressions
Wicker et al. 2003) n = 14 (0%)	20–27	Participants watched facial expressions of disgust and pleasure	Neutral expressions
Wolf et al. 2010 n = 18	20–45	Judgment of mental states from a movie (Dziobek et al. 2006)	Physical details
Young et al. 2007 n = 27 (44%)	18–22	Participants judged belief states of a protagonist	False photograph stories
Young et al. 2010 n = 17 (41%)	18–31	False belief stories	False photograph stories
Young et al. 2011 n = 17 (59%)	18–22	False belief stories (Saxe and Kanwisher 2003)	False photographs or maps
Zaitchik et al. 2010 n = 15 (47%)	22.4 (20–24)	Participants judged beliefs and emotional states	Syntax control condition
Zhang et al. 2018 n = 25 (52%)	20.9 (19–24)	Participants judged emotions from facial expressions and vocal prosody	Neutral faces and prosody

(*continued on next page*)

Table 3 (*continued*)

Author Participants (% female)[a]	Age[b]	Experimental task	Control task
Zheng et al., 2016 n = 20 (50%)	25.0 ± 1.6	Participants watched painful stimuli	Non-painful stimuli
Zheng et al., 2016 n = 20 (60%)	21.7 ± 1.9	Participants watched painful stimuli	Non-painful stimuli
Ziaei et al. 2016 n = 40	20.7 ± 2.7 (n = 20) 69.8 ± 3.0 (n = 20)	Reading the mind in the eyes task (Baron-Cohen et al. 2001)	Gender discrimination task

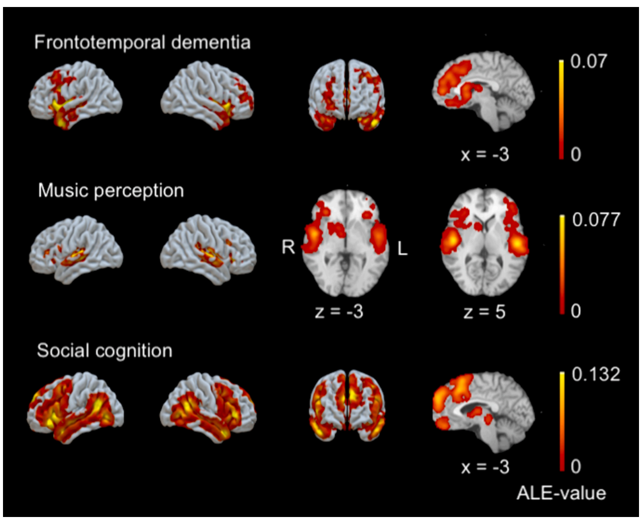

Fig. 1. Meta-analytic results of brain regions involved in atrophy of FTD and functional activity during music perception and social cognition tasks. z = axial location of x,y,z coordinates. x = sagittal location of x,y,z coordinates. The ALE-scores are demonstrated. For the coordinates and brain regions see Table S4, S8-9. All results were thresholded at cluster-wise threshold $p < 0.05$ (FWE-corrected).

Our results were in line with previous research for the observed atrophy patterns in FTD (C. Luo et al. 2020; Pan et al. 2012; Schroeter et al. 2007, 2008; Yang et al. 2012) and functional activity in music perception (Janata 2015; Limb 2006). The observed functional activity pattern in social cognition was similar to previous meta-analyses on Theory of Mind (Molenberghs et al. 2016; Schurz et al. 2014). Unlike these studies, we only observed activation in the precuneus in the Theory of Mind subgroup analysis, but not general social cognition. This suggests that activation in the precuneus might be specific for Theory of Mind tasks.

Our study extends the literature by demonstrating evidence for a potential relationship between the three modalities. We found that neuronal circuits showing atrophy in FTD patients are also functionally involved in music perception and social cognition. This provides a putative biological substrate for alterations in music perception and social cognition observed clinically. The shared anatomical areas in music perception and social cognition extended from the caudal part of the superior temporal gyrus (BA 21) rostrally to the inferior frontal gyrus (BA 47). This neuronal circuit was also observed in the conjunction analysis of FTD and social cognition and thus appears to play a central role in all three modalities. In the left hemisphere these brain areas are part of the 'ventral language pathway' that extends from the auditory cortex through the insula to the inferior frontal gyrus (Saur et al. 2008), and is known to be involved in higher-level language processing having mainly a sound-to-meaning function (Aryani et al. 2019; Berwick et al. 2013; Frühholz et al. 2016; Saur et al. 2008). Atrophy in most of these

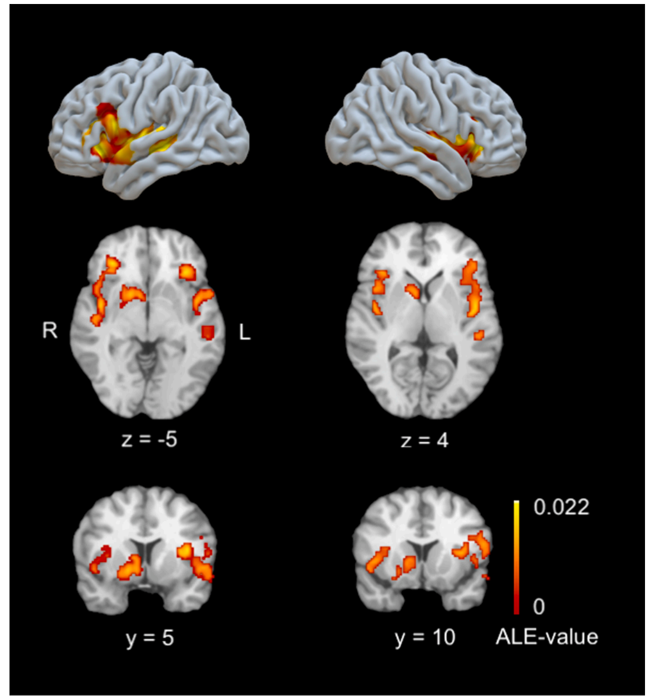

Fig. 2. Brain regions involved in the conjunction analysis of FTD and music perception. z = axial location of x,y,z coordinates. y = coronal location of x,y,z coordinates. The ALE-scores are demonstrated. For the coordinates and brain regions see Table 4. All results were thresholded at a cluster-wise threshold of $p < 0.05$ (FWE-corrected).

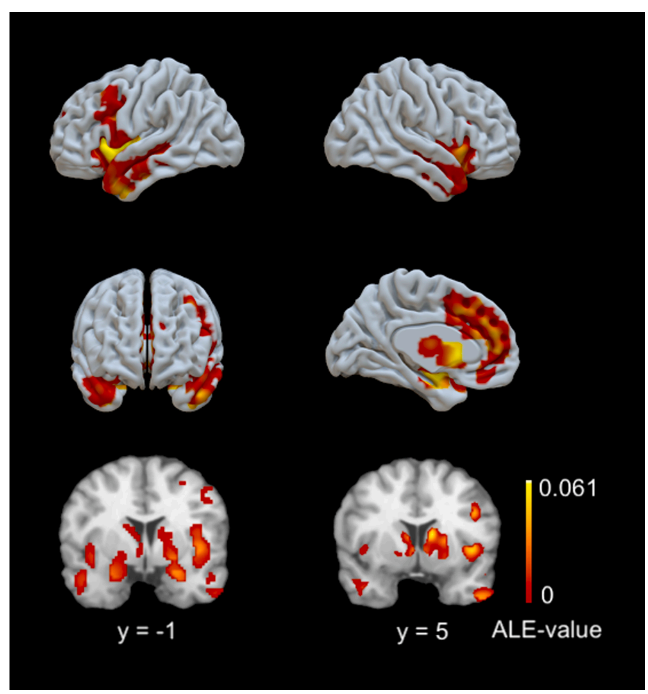

Fig. 3. Brain regions involved in the conjunction analysis of FTD and social cognition. y = coronal location of x,y,z coordinates. The ALE-scores are demonstrated. For the coordinates and brain regions see Table 4. All results were thresholded at a cluster-wise threshold of $p < 0.05$ (FWE-corrected).

brain areas were previously reported to be related to a loss of sarcasm recognition as part of social cognition tasks in FTD (Downey et al. 2015). Oechslin et al. reported that the ventral pathway in the right hemisphere

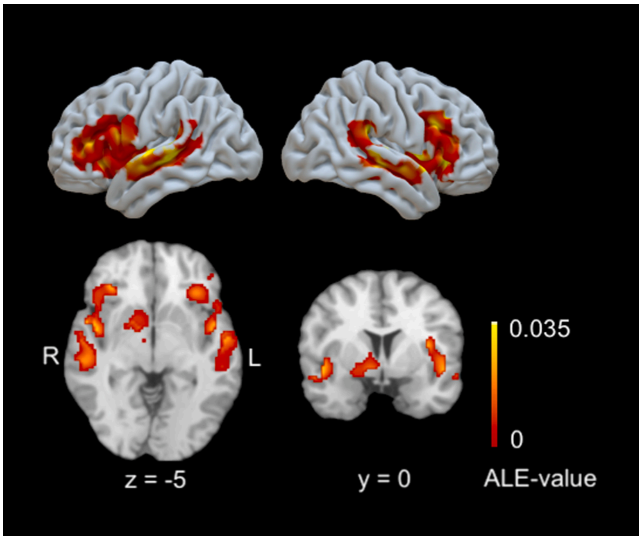

Fig. 4. Brain regions involved in the conjunction analysis of music perception and social cognition. z = axial location of x,y,z coordinates. y = coronal location of x,y,z coordinates. The ALE-scores are demonstrated. For the coordinates and brain regions see Table 4. All results were thresholded at a cluster-wise threshold of $p < 0.05$ (FWE-corrected).

was functionally involved in music syntax processing in musicians (Oechslin et al. 2017). Other studies found similar brain regions involved in affective voice processing (Leitman et al. 2010; Regenbogen et al. 2012; Zhang et al. 2018). Together with our results, this suggests that brain regions involved in interpreting sounds of social cognition and music may share a neurobiological basis bilaterally, and could explain loss of these functions in FTD. Of note is that the studies we included in this meta-analysis for social cognition used different test paradigms, which did not necessarily aim at the interpretation of voices. The observation that this pathway was robustly implied with social cognition suggests that it might be a key circuit for social cognition. All three modalities further demonstrated an anatomical overlap in mesolimbic dopaminergic circuits which are also known to be involved in reward and behavior (Omar et al. 2011; Salimpoor et al. 2011; Zatorre and Salimpoor 2013) and basal forebrain and striatal regions that are part of the semantic appraisal network which is involved in weighing hedonic value of (social and asocial) stimuli (Ranasinghe et al. 2016; Seeley et al. 2012; Zhou and Seeley 2014). These findings possibly explain the altered rewarding sensation that patients with FTD can experience when listening to music (i.e. musicophilia or sound-aversion; Fletcher et al. 2013; Omar et al. 2011). Of note, in the subgroup analyses we only found these regions activated in bvFTD as opposed to other FTD subtypes, possibly accounting for the effect on the pooled data.

We further found the strongest correlation of FTD and music perception in the insulae, which is in line with a previous report of involvement of the insula and putamen involved in hedonic musical changes in FTD (P. D. Fletcher et al. 2015). This activation was present in all FTD subtypes. Since the insula is one of the first brain areas that are affected in patients with FTD (Broe et al. 2003; Buhour et al. 2016), the reported changes in music perception could be an early indication of neurodegenerative processes in FTD, and possibly play a role in altered social cognitive abilities. Future research should further scrutinize the shared neurobiological mechanisms of music and social cognition in the disease pathogenesis of FTD.

A previous study by Seeley et al. observed that the brain regions atrophied in FTD are part of the functionally defined salience network, which has been shown to be disrupted in FTD patients and is important for complex social behavior (Seeley et al. 2009; Zhou et al. 2010). This network connects the insula and cingulate gyrus with the amygdala, thalamus and striatal regions. Our results show that atrophy patterns

Table 4
Results of the conjunction analyses. Illustrated are the clusters, the total volume of each cluster, x,y,z peak-coordinates and brain area. BA = Brodmann area.

Cluster	Volume (mm^3)	x	y	z	Label
Conjunction analysis of frontotemporal dementia and music perception					
1	9480	–32	14	10	Left insula BA 13
		−36	4	14	Left insula BA 13
		−36	24	10	Left inferior frontal gyrus BA 13
		–32	24	−4	Left inferior frontal gyrus BA 47
		−44	−2	0	Left insula BA 13
		−42	−10	4	Left insula BA 13
		−30	4	10	Left claustrum
		−42	30	4	Left inferior frontal gyrus BA 13
		−54	6	−10	Left superior temporal gyrus BA 38
		−46	12	4	Left insula BA 13
2	6552	32	32	−4	Right inferior frontal gyrus BA 47
		42	−4	−2	Right insula BA 13
		42	−10	2	Right insula BA 13
		36	22	8	Right inferior frontal gyrus BA 13
		44	−18	−2	Right insula BA 13
		34	26	−6	Right inferior frontal gyrus BA 47
		42	12	2	Right insula BA 13
		46	6	−4	Right insula BA 22
		46	12	−4	Right inferior frontal gyrus BA 47
		40	14	8	Right insula BA 13
		42	20	−6	Right inferior frontal gyrus BA 47
		34	12	16	Right insula BA 13
3	2536	16	4	−4	Right globus pallidus
		8	4	−4	Right caudate head
		8	6	2	Right caudate head
		10	6	6	Right caudate body
4	1512	−52	10	18	Left inferior frontal gyrus BA 44
		−50	12	24	Left inferior frontal gyrus BA 9
		−54	8	12	Left precentral gyrus BA 44
		−38	18	20	Left middle frontal gyrus BA 46
		−46	20	28	Left middle frontal gyrus BA 9
		−42	8	24	Left inferior frontal gyrus BA 9
5	1208	−52	−26	−2	Left superior temporal gyrus BA 21
		−46	−32	6	Left superior temporal gyrus BA 22
Conjunction analysis of frontotemporal dementia and social cognition					
Cluster	**Volume (mm^3)**	**x**	**y**	**z**	**Label**
1	27,432	−36	18	0	Left insula BA 13
		–22	−6	−14	Left amygdala
		−10	8	10	Left caudate body
		−40	2	0	Left insula BA 13
		−42	6	28	Left inferior frontal gyrus BA 9
		−46	8	−34	Left middle temporal gyrus BA 21
		−20	0	−6	Left lateral globus pallidus
		−20	4	6	Left putamen
		−48	12	−20	Left superior temporal gyrus BA 38
		−38	2	12	Left insula BA 13
		–32	32	−4	Left inferior frontal gyrus BA 47
		−54	8	8	Left precentral gyrus BA 44
		−38	−2	−12	Left superior temporal gyrus BA 21
		−46	0	38	Left middle frontal gyrus BA 6
		−52	10	18	Left inferior frontal gyrus BA 44

(*continued on next page*)

Table 4 (*continued*)

Cluster	Volume (mm³)	x	y	z	Label
Conjunction analysis of frontotemporal dementia and music perception					
2	15,144	−4	50	8	Left medial frontal gyrus BA 10
		0	40	32	Left medial frontal gyrus BA 9
		0	38	36	Left medial frontal gyrus BA 6
		−6	16	40	Left cingulate gyrus BA 32
		−4	48	20	Left medial frontal gyrus BA 9
		0	26	44	Left medial frontal gyrus BA 8
		−4	30	24	Left anterior cingulate gyrus BA 32
		6	10	46	Right medial frontal gyrus BA 32
		−6	40	24	Left medial frontal gyrus BA 9
		−12	8	52	Left medial frontal gyrus BA 6
3	10,552	34	18	−16	Right inferior frontal gyrus BA 47
		34	20	−8	Right inferior frontal gyrus BA 47
		36	18	−4	Right inferior frontal gyrus BA 47
		38	10	–32	Right superior temporal gyrus BA 38
		40	−6	−4	Right insula BA 13
		44	20	−30	Right superior temporal gyrus BA 38
		48	−2	–22	Right fusiform gyrus BA 20
		48	8	–22	Right superior temporal gyrus BA 38
		34	30	−4	Right inferior frontal gyrus BA 47
4	4368	24	−8	−14	Right amygdala
		10	8	10	Right caudate body
		4	6	0	Right caudate head
		18	4	−4	Right putamen
5	1736	−54	−12	–22	Left inferior temporal gyrus BA 20
		−64	−10	−16	Left inferior temporal gyrus BA 21
6	1600	−52	−28	−4	Left middle temporal gyrus BA 21
7	736	0	−10	12	Left thalamus
8	488	0	38	−12	Left medial frontal gyrus BA 11
9	264	−40	16	48	Left superior frontal gyrus BA 8
10	256	46	−18	−8	Right superior temporal gyrus BA 22
Conjunction analysis of music perception and social cognition					
Cluster	**Volume (mm³)**	**x**	**y**	**z**	**Label**
1	12,312	32	28	−2	Right inferior frontal gyrus BA 47
		52	4	−4	Right superior temporal gyrus BA 22
		44	−4	−4	Right insula BA 13
		46	−2	−8	Right superior temporal gyrus BA 22
		52	−24	2	Right superior temporal gyrus BA 22
		50	–22	−2	Right superior temporal gyrus BA 21
		42	20	30	Right middle frontal gyrus BA 9
		54	−10	−6	Right superior temporal gyrus BA 22
		56	−6	−6	Right middle temporal gyrus BA 21
		54	−2	−10	Right middle temporal gyrus BA 21
		52	−16	−4	Right superior temporal gyrus BA 22
		52	−28	−6	Right middle temporal gyrus BA 21
		60	−32	4	Right middle temporal gyrus BA 22
		48	26	8	Right inferior frontal gyrus BA 45
		50	−2	−12	Right middle temporal gyrus BA 21
		36	22	10	Right insula BA 13
		42	12	4	Right insula BA 13
		58	20	22	Right inferior frontal gyrus BA 9
		42	22	−6	Right inferior frontal gyrus BA 47
		44	16	−6	Right inferior frontal gyrus BA 47
2	11,200	−54	8	20	Left inferior frontal gyrus BA 44
		–32	14	12	Left insula BA 13
		−46	−2	−4	Left superior temporal gyrus BA 22
		−38	24	10	Left inferior frontal gyrus BA 13
		−34	0	12	Left insula BA 13
		−42	38	6	Left inferior frontal gyrus BA 46
		–32	24	−4	Left inferior frontal gyrus BA 47
		−46	30	8	Left inferior frontal gyrus BA 46
		−44	20	28	Left middle frontal gyrus BA 9
		−42	26	16	Left middle frontal gyrus BA 46
		−40	26	20	Left middle frontal gyrus BA 46
		−46	12	6	Left insula BA 13
		−42	8	24	Left inferior frontal gyrus BA 9
		−48	16	−6	Left inferior frontal gyrus BA 47
3	4144	−54	−26	2	Left superior temporal gyrus BA 22
		−54	–22	0	Left superior temporal gyrus BA 21
		−54	−12	−4	Left superior temporal gyrus BA 22
		−54	−6	−6	Left superior temporal gyrus BA 22
		−56	−42	20	Left superior temporal gyrus BA 13
4	2216	12	4	−4	Right globus pallidus
		10	6	2	Right caudate head
		10	−2	−4	Right medial globus pallidus
5	1736	50	−40	22	Right insula BA 13
		62	−40	22	Right superior temporal gyrus BA 22

observed in FTD mirror this network. Furthermore, we found that many of these regions are involved in music perception and social cognition. Dysfunction of this network is previously found to express with typical social-emotional problems (Farb et al. 2013; Rosen et al. 2002) just as music-emotion recognition (Omar et al. 2011) and musicophilia (Fletcher et al. 2013) in FTD patients. Finally, our subgroup analyses showed similar patterns of activation in FTD with both empathy and social cognition, particularly in the salience network. Our results provide further insight into social-emotional behavioral disturbances in FTD patients. These results have promising implications for the clinical applications of music as a probe for social cognitive and socio-emotional disturbances in diseases where these are most salient.

A potential limitation of our study is the translation of reported foci to voxels, which may have introduced noise into the results. The same principle applies to combining the data of structural and functional imaging studies. Another general limitation is heterogeneity of the included studies. A minority of studies investigated genetic and anatomical variants of FTD. To improve statistical power we included studies with and without control conditions in the music perception group. Furthermore, as all the studies we included for music perception were listening tasks, and thus relatively homogenous in terms of tasks studied in contrast to social cognition. It is worth mentioning that the included studies predominantly used western music on western participants, and so it remains uncertain whether our conclusions are generalizable to non-western populations. A strength of our research was the large number of individuals that were included across all studies. Furthermore, we demonstrated an insightful and unique approach in investigating common neurobiological circuits by performing conjunction analyses on meta-analytic data.

5. Summary

Our meta-analysis demonstrates that music perception and social cognition share neurobiological circuits in frontotemporal dementia. This suggests music could be a sensitive probe for social cognition abilities with implications for diagnosis and monitoring.

CRediT authorship contribution statement

Jochum J. van't Hooft: Conceptualization, Investigation, Writing - original draft, Writing - review & editing, Visualization. **Yolande A.L. Pijnenburg:** Conceptualization, Writing - review & editing. **Sietske A. M. Sikkes:** Writing - review & editing. **Philip Scheltens:** Writing - review & editing. **Jacoba M. Spikman:** Writing - review & editing. **Artur C. Jaschke:** Writing - review & editing. **Jason D. Warren:** Writing - review & editing. **Betty M. Tijms:** Supervision, Conceptualization, Software, Writing - review & editing, Project administration, Resources.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bandc.2020.105660.

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