Structural connectivity of right frontal hyperactive areas scales with stuttering severity

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Supplementary material

Supplementary Table 1 Individual characteristics of control participants

ID	Sex	Age	LQ	Edu	History	%SS
C1	m	24	100	4	none	0
C2	m	26	100	5	none	0.3
C3	m	52	100	6	none	0
C4	m	36	100	6	none	0
C5	m	25	80	5	none	0
C6	m	26	80	5	none	0.4
C7	m	36	100	6	none	0
C8	m	27	100	6	none	0
C9	m	23	100	4	none	0
C10	m	47	75	1	none	0.1
C11	m	39	100	5	none	0.1
C12	m	56	100	6	none	0.1
C13	m	53	95	2	none	0.1
C14	m	30	100	6	none	0
C15	m	20	95	3	none	0
C16	m	57	100	1	none	0
C17	m	62	100	6	none	0.4
C18	f	24	100	3	none	0
C19	f	24	80	3	none	0
C20	f	24	100	4	none	0
C21	f	27	100	6	none	0
C22	f	27	80	6	none	0
C23	f	22	80	3	none	0
C24	f	42	100	1	none	0
C25	f	35	100	6	none	0
C26	f	48	100	2	none	0
C27	f	28	75	3	none	0
C28	f	57	100	1	none	0.2
C29	f	51	100	1	none	0
C30	f	49	95	1	none	0
C31	f	29	100	4	none	0
C32	f	46	95	1	none	0
C33	f	42	100	1	none	0
C34	f	46	100	1	none	0

LQ = laterality quotient (Oldfield, 1971), Edu = education, History = family history of stuttering, %SS = stuttered syllables occurring per 100 syllables across 1000 syllables (reading and free production)

Supplementary Table 2 Individual characteristics of adults who stutter

ID	Sex	Age	LQ	Edu	History	ASO	SSI-4			OASES						
							%SS	SSI	Severity	GI	RS	CDS	QL	Total	Miss	Severity
S1	m	27	80	5	m	6	1.3	8	disclosed*	53.0	48.0	53.3	30.8	46.3	1	moderate
S2	m	23	80	3	none	4	69.6	40	very severe	72.0	83.3	90.0	75.8	80.3	1	severe
S3	m	50	100	6	u	4	3.9	14	very mild	27.0	0.0	0.0	0.0	6.8	90	n/a
S4	m	63	70	6	u	6	2.4	12	very mild	45.0	39.3	36.7	32.5	38.4	0	mild-to-moderate
S5	m	36	60	1	f, c	5	3	19	mild	40.0	28.7	26.7	25.8	30.3	0	mild-to-moderate
S6	m	42	100	6	b	4	1	10	very mild	45.0	44.7	48.3	39.2	44.3	1	mild-to-moderate
S7	m	27	100	5	b	9	2.3	19	mild	56.0	52.7	53.3	59.2	55.3	1	moderate
S8	m	52	95	6	n/a	3	0.9	4	disclosed*	56.0	63.3	44.2	54.2	54.4	0	moderate
S9	m	26	100	4	gm	4	2.4	13	very mild	49.0	48.0	51.7	48.3	49.3	0	moderate
S10	m	47	100	6	m, gm	4	0.8	7	disclosed*	41.0	39.3	30.8	28.3	34.9	0	mild-to-moderate
S11	m	55	100	1	none	4	1.5	12	very mild	49.0	56.7	50.0	45.0	50.2	1	moderate
S12	m	19	75	1	none	5	2.3	11	very mild	52.0	56.0	55.8	65.0	57.2	1	moderate
S13	m	30	90	6	none	3	49.1	43	very severe	56.0	54.7	40.0	35.0	46.4	3	moderate
S14	m	38	95	6	f	3	7.9	22	mild	43.0	58.0	61.7	47.5	52.5	1	moderate
S15	m	38	100	6	none	4	0.2	0	disclosed*	61.0	40.0	48.3	37.5	46.7	1	moderate
S16	m	24	100	4	f, b	4	12.0	34	severe	59.0	55.3	51.7	40.0	51.5	10	moderate
S17	f	22	100	3	f	3	23.3	36	severe	53.0	45.3	53.3	36.7	47.1	1	moderate
S18	f	25	100	4	u	3	1.3	7	disclosed*	58.0	67.3	72.5	61.7	64.9	0	moderate-to-severe
S19	f	47	100	6	n, c	3	0.1	0	disclosed*	32.0	25.3	25.0	21.7	26.0	0	mild
S20	f	20	100	1	a	4	3.3	17	very mild	47.0	38.7	45.0	32.5	40.8	3	mild-to-moderate
S21	f	30	100	1	none	4	13.1	31	moderate	57.0	58.0	60.8	54.2	57.5	1	moderate
S22	f	32	90	1	none	5	9.8	20	mild	27.0	24.7	25.0	22.5	24.8	0	mild
S23	f	22	70	5	f, b	1	2.2	13	very mild	33.0	41.3	33.3	26.7	33.6	1	mild-to-moderate
S24	f	50	85	6	f	5	0.3	0	disclosed	48.0	63.3	62.5	51.7	56.4	1	moderate
S25	f	43	100	6	gc	9	1.2	12	very mild	35.0	34.0	26.7	21.7	29.3	0	mild-to-moderate
S26	f	38	100	6	C	3	4.2	25	moderate	54.0	51.3	60.0	49.2	53.6	1	moderate
S27	f	58	100	6	f, b	2	10.9	22	mild	39.0	48.7	48.3	36.7	43.2	0	mild-to-moderate
S28	f	52	100	6	f, b	7	0.5	4	disclosed*	47.0	47.3	44.2	45.0	45.9	1	moderate
S29	f	29	100	6	f, u	4	7.5	21	mild	51.0	43.3	26.7	28.3	37.3	0	mild-to-moderate
S30	f	36	100	1	u, s	3	1.8	14	very mild	52.0	54.0	50.0	51.7	51.9	1	moderate
S31	f	36	80	1	m, u, ch	5	3.8	24	mild	43.0	40.0	36.7	25.0	36.2	2	mild-to-moderate

LQ = laterality quotient (Oldfield, 1971); Edu = education; History = family history of stuttering, m = mother, f = father, b = brother, s = son, ch = children, gm = grandmother, gf = grandfather, u = uncle, a = aunt, n = nephew, c = cousin, gc = grand; ASO = age of stuttering onset in years; %SS = stuttered syllables occurring per 100 syllables across 1000 syllables (reading and free production), SSI = total score in the stuttering severity index (SSI-4), *disclosed = SSI-4 does not give a diagnosis of stuttering but participants reported their history

of stuttering and disclosed continuing stuttering; OASES = Overall Assessment of Speaker's Experience of Stuttering (Yaruss and Quesal, 2006), given are impact scores of all subsections: GI = general information, RS = reaction to stuttering, CDS = communication in daily life, QL = quality of life, Total = total impact score, Miss = items not completed out of 100.

Supplementary Table 3 Brain activation across all participants in speaking > humming

Brain area	MNI-coordinates			Extent	*z*-score
	x	y	z	(voxels)	($z > 3.5$, $\alpha < 0.05$)
R Anterior intra-parietal sulcus (hIP1)	38	-56	46	2116	7.06
➢ R Inferior parietal lobule (PF)	50	-36	44		6.85
➢ R Inferior parietal lobule (PGp)	42	-76	38		6.64
L Premotor cortex (BA 6)	-52	-6	40	1920	7.58
➢ L Primary motor cortex (BA 4p)	-54	-4	30		6.63
➢ L Inferior frontal cortex (BA 44)	-40	2	28		6.43
R Paracingualte gyrus	10	16	48	1031	6.85
➢ L Supplementary motor area (BA 6)	-6	4	56		6.67
L Middle temporal gyrus	-48	-46	8	745	7.32
➢ L Superior temporal gyrus	-66	-18	6		5.74
L Anterior intra-parietal sulcus (hIP3)	-30	-54	42	673	6.82
➢ L Anterior intra-parietal sulcus (hIP2)	-46	-38	40		6.29
➢ L Inferior parietal lobule (PGp)	-32	-74	36		4.83
R Middle frontal gyrus	34	2	56	517	6.87
R Insula	32	20	2	422	6.66
R Frontal pole	38	36	32	342	5.57
➢ R Middle frontal gyrus (BA 9)	40	38	28		5.56
R Inferior temporal gyrus	56	-44	-12	204	5.97
➢ R Middle temporal gyrus, posterior	64	-28	-10		4.97
R Cerebellum, VI	18	-58	-26	155	6.44
L Inferior temporal gyrus	-52	-56	-12	155	5.86
R primary motor cortex (BA 4p)	48	-8	38	143	5.37
➢ R Somatosensory cortex (BA 3a)	46	-10	30		4.68
R Occipital pole	20	-94	4	111	6.18
R Thalamus	12	-14	12	89	5.23
L Thalamus	-12	-16	10	86	5.35

Supplementary Table 4 Brain activation across all participants in humming > speaking

Brain area	MNI-coordinates			Extent (voxels)	*z*-score ($z > 3.5$, $\alpha < 0.05$)
	x	y			
L Lateral occipital cortex	-24	-88	18	4404	8.96
➢ L Occipital fusiform gyrus	-14	-86	-10		8.44
R Lateral occipital cortex	36	-76	14	1435	8.16
➢ R Occipital pole					
L Frontal orbital cortex	-40	32	-14	1377	7.1
➢ L Frontal orbital cortex	-44	32	-12		7.01
➢ L Inferior frontal gyrus (BA 45)	-46	46	0		6.87
L Middle frontal gyrus	-28	26	50	802	6.02
➢ L Superior frontal gyrus	-24	34	48		5.6
L Frontal pole	-6	58	18	750	6.09
➢ L Frontal medial cortex	-2	50	-8		5.6
➢ L Paracingulate gyrus	-4	54	2		5.46
L Planum polare/primary auditory cortex (TE1.2)	-50	0	-4	617	6.76
➢ L temporal pole	-34	6	-20		6.61
➢ L Insula	-40	-8	-8		6.02
➢ L Frontal orbital cortex	-28	14	24		4.83
L Precuneus	-8	-50	38	528	5.91
➢ L Cingulate gyrus, posterior	-4	-52	26		5.28
L Occipital fusiform gyrus	26	-64	-8	526	6.98
➢ L Temporal occipital fusiform cortex	28	-56	-10		6.33
L Inferior parietal lobule (PFm)	-44	-58	28	478	5.55
➢ L Inferior parietal lobule (PFm)	-56	-54	38		5.45
➢ L Inferior parietal lobule (PGa)	-50	-56	28		5.41
R Inferior frontal gyrus (BA45)	52	34	4	178	7.42
R Insula	40	6	-16	118	5.62
➢ R Temporal pole	54	10	-14		5.55
L Cingulate gyrus, anterior	0	-12	40	84	5.6

Supplementary Table 5 Brain activation in controls in speaking > humming

Brain area	MNI-coordinates			Extent (voxels)	*z*-score ($z > 3.5$, $\alpha < 0.05$)
	x	y			
L Middle temporal gyrus	-50	-48	6	3645	6.78
➢ L Primary somatosensory cortex (BA 3b)	-50	-12	42		5.86
➢ L Primary motor cortex (BA 4p)	-54	-2	28		5.45
➢ L Premotor cortex (BA 6)	-54	2	24		5.43
➢ L Superior temporal gyrus, posterior	-54	-30	4		5.11
R Inferior parietal lobule (PFm)	48	-40	44	2381	5.38
➢ R Inferior parietal lobule PGp	36	-74	46		5.34
➢ R Anterior intra-parietal sulcus (hIP3)	34	-58	42		4.98
L Supplementary motor area (BA 6)	-4	6	52	1034	5.46
➢ L Paracingulate gyrus	-6	16	40		3.95
➢ R Paracingulate gyrus	6	16	48		5.22
L Inferior parietal lobule (Pga)	-30	-66	46	690	5.57
➢ L anterior intra-parietal sulcus (hIP3)	-30	-52	44		4.99
➢ L anterior intra-parietal sulcus (hIP2)	-46	-38	40		4.67
➢ L anterior intra-parietal sulcus (hIP1)	-32	-46	36		4.3
➢ L Inferior parietal lobule PGp	-32	-70	36		3.75
➢ L Primary somatosensory cortex (BA 1)	-52	-30	56		3.6
R Middle frontal gyrus	32	2	60	354	4.8
L Inferior temporal gyrus	-56	-58	-16	312	5.37
R Inferior temporal gyrus	64	-52	-16	232	5.18
➢ R Middle temporal gyrus, posterior	62	-36	-14		3.63
R Insula	32	20	8	173	4.39
R Precuneus	10	-68	48	165	4.97
L Thalamus	-8	-14	14	200	4.54
R Thalamus	10	22	14	253	4.58
R Cerebellum (VI)	18	-60	-24	335	4.95

Supplementary Table 6 Brain activation in controls in humming > speaking

Brain area	MNI-coordinates			Extent (voxels)	*z*-score ($z > 3.5$, $\alpha < 0.05$)
	x	y			
L Lateral occipital cortex	-24	-86	20	5546	6.85
➢ L Occipital fusiform gyrus	-16	-86	-12		6.18
R Lateral occipital cortex	34	-78	14	1954	6.58
➢ R Occipital pole	12	-92	14		5.38
L Frontal orbital cortex	-24	32	-12	1734	5.92
➢ L Frontal pole	-48	48	-2		5.21
L Planum polare/primary auditory cortex (TE1.2)	-50	0	-4	813	5.71
➢ L Temporal pole	-34	6	-18		4.94
➢ L Parahippocampal gyrus/Amygdala superficial	-26	2	-22		4.51
➢ L Temporal fusiform cortex	-32	-2	-36		4.11
R Temporal occipital fusiform cortex	30	-56	-8	701	5.34
L Frontal pole	-10	60	18	615	4.75
➢ L Frontal medial cortex	-4	50	-8		3.99
R Inferior frontal gyrus (BA 45)	50	34	6	587	5.95
➢ R Frontal pole	40	34	-10		4.59
R Inferior parietal lobule (PF)	60	-26	30	527	4.88
➢ R Superior temporal gyrus, posterior	66	-32	16		3.72
R Temporal pole	38	6	-18	256	4.41
➢ R Parahippo gyrus/Hippo entorhinal cortex	28	-2	-34		4.05
➢ R Amygdala, superficial	30	4	-28		3.71
➢ R Amygdala, laterobasal	26	-6	-20		3.66

Supplementary Table 7 Brain activation in AWS in speaking > humming

Brain area	MNI-coordinates			Extent (voxels)	*z*-score ($z > 3.5$, $\alpha < 0.05$)
	x	y			
R Anterior intra-parietal sulcus (hIP3)	40	-54	48	1651	5.39
➢ R Inferior parietal lobule (PF)	52	-36	44		4.93
➢ R Anterior intra-parietal sulcus (hIP1)	44	-42	44		4.69
➢ R Inferior parietal lobule (PGp)	42	-76	38		4.67
➢ R Anterior intra-parietal sulcus (hIP2)	44	-38	48		4.63
R Middle frontal gyrus	34	4	56	1477	4.96
➢ R Paracingulate gyrus	10	16	48		4.84
➢ L Supplementary motor area	-8	0	58		4.81
➢ R Superior frontal gyrus	22	10	58		4.26
R Insula	32	20	2	1359	5.06
➢ R Inferior frontal gyrus (BA 44)	50	6	30		4.93
➢ R Frontal operculum cortex	34	18	12		4.6
➢ R Primary motor cortex (BA 4p)	46	-8	38		4.42
➢ R Inferior frontal gyrus (BA 44)	52	10	14		4.25
R Frontal pole	36	46	0	1342	4.88
➢ R Middle frontal gyrus (BA 9)	36	38	32		4.14
L Premotor cortex (BA 6)	-54	-6	40	1233	5.32
L Anterior intra-parietal sulcus (hIP3)	-28	-54	40	666	5.17
➢ L Anterior intra-parietal sulcus (hIP1)	-34	-54	44		5.07
➢ L Anterior intra-parietal sulcus (hIP2)	-48	-38	40		4.29
L Superior temporal gyrus, posterior	-50	-42	8	494	5.46
➢ L Inferior temporal gyrus	-50	-52	-12		4.44
R Middle temporal gyrus, posterior	64	-28	-10	274	4.52
L Insula	-32	16	8	199	4.17

Supplementary Table 8 Brain activation in AWS in humming > speaking

Brain area	MNI-coordinates			Extent (voxels)	*z*-score ($z > 3.5$, $\alpha < 0.05$)
	x	y			
L Occipital fusiform gyrus	-18	-80	-10	3172	7.22
➢ L Occipital pole	-26	-90	16		6.14
➢ L Lateral occipital cortex	-34	-88	12		5.56
L Middle frontal gyrus	-28	28	48	2324	4.91
➢ L Paracingulate gyrus	-6	54	22		4.78
➢ L Superior frontal gyrus	-20	32	50		4.78
L Frontal orbital cortex	-46	30	-12	1478	4.93
➢ L Temporal pole	-40	4	-18		4.73
➢ L Inferior frontal gyrus (BA 45)	-46	46	0		4.69
➢ L Inferior frontal gyrus (BA 45)	-52	34	6		4.36
➢ L Planum polare/primary auditory cortex (TE1.2)	-52	0	-4		4.39
L Precuneus	-8	-44	40	1068	5.57
➢ L Cingulate gyrus, posterior	-4	-48	24		3.97
L Inferior parietal lobule (PFm)	-54	-56	46	911	5.05
➢ L Inferior parietal lobule (Pga)	-54	-60	42		4.96
R Lateral occipital cortex	38	-78	14	861	5.17
➢ R Occipital pole	10	-92	12		3.89
R Occipital fusiform gyrus	26	-68	-8	479	4.96
➢ R Lingual cortex	20	-42	-14		3.95
R Temporal pole	56	10	-14	333	5.2
L Lateral occipital cortex	-10	-84	42	175	4.39

Supplementary discussion on the lack of a hypo-activity of the left posterior IFG in adults who stutter compared to fluent speakers

In our previous study, where we used the same paradigm, we report and discuss a hypo-activation of the left posterior IFG in adults who stutter compared to fluent speakers (Neef *et al.*, 2016). It is important to note that there were essential differences between the current study and our previous study. (1) In this previous study, the differences of activity in the IFG resulted from region of interest analyses separated for imagining humming and imagining speaking. However, the whole-brain analysis, which requires a more stringent correction for multiple testing, resulted in no group differences. (2) Furthermore, in the previous study we analyzed data from 17 fluently speaking males and 16 males who stutter. In the current study we have more power because we analyze data from 31 adults who stutter and 34 fluent speakers. This might be the primary reason why a whole-brain analysis yielded hyperactivity in the right hemisphere of adults who stutter when compared to fluent speakers.

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