Hypothalamic dysfunction revealed by magnetic resonance diffusion tensor imaging in childhood leukemia survivors treated with cranial radiotherapy but not in craniopharyngioma survivors

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Conclusion

34 years after CRT and chemotherapy, DTI detects hypothalamic dysfunction in ALL survivors

The survivors with overweight were presented with worse hypothalamic damage compared to survivors with normal weight. While CP without HT tumour involvement survivors seemed to be unaffected, the present data suggests important hypothalamic dysfunction after CRT in ALL survivors

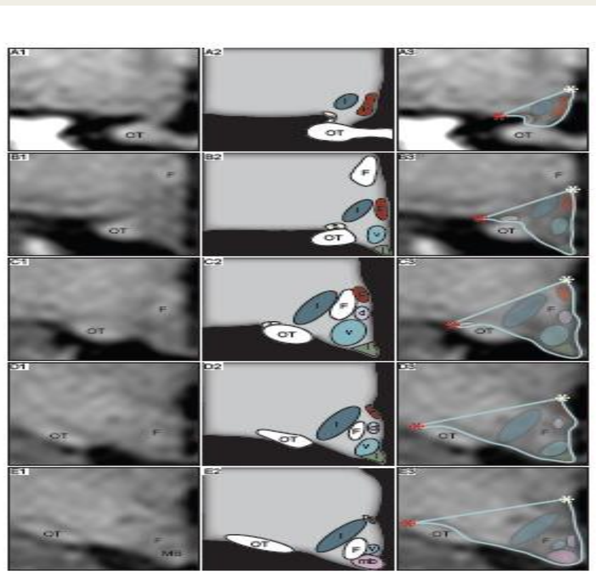
Background

- Metabolic complications, including obesity, are frequent in acute lymphoblastic leukemia (ALL) survivors treated with cranial radiotherapy (CRT) in childhood
- Such complications are potentially mediated by the hypothalamus (HT), a regulator of energy expenditure
- Childhood onset (CO) Craniopharyngioma (CP) survivors without HT involvement are often spared gross obesity problems
- Magnetic resonance diffusion tensor imaging (DTI) provides information on the tissue microstructure of the brain as quantified by its parameters fractional anisotrophy (FA), mean diffusivity (MD), axial diffusivity (AD), radial diffusivity (RD)

Aim

Since MD in the HT is reportedly increased in obese compared to non-obese subjects, we investigated DTI in the HT in these two patient populations to find out HT´s involvement in the obesity in ALL survivors

Delineation of the hypothalamus



Participants

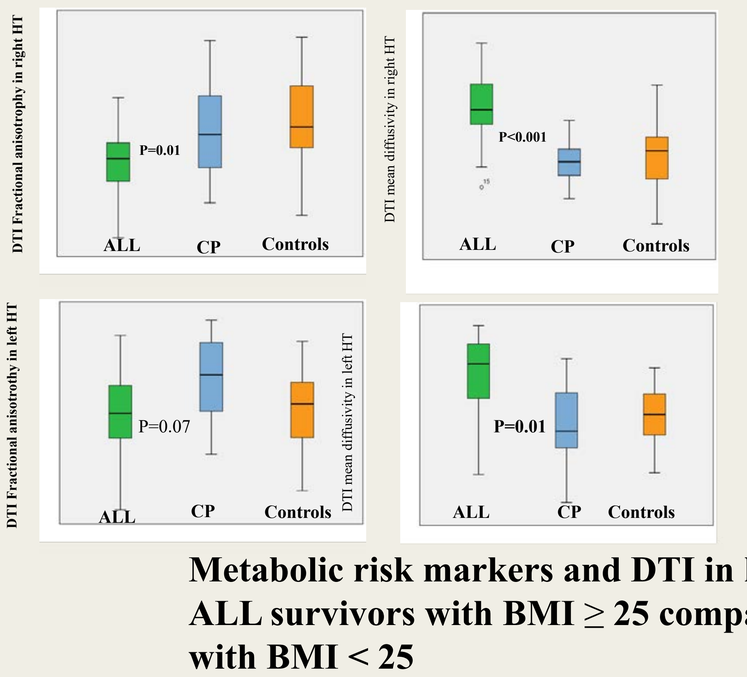
- 27 ALL survivors (median age 34 years (27-46 years), treated with a CRT dose of 24 Gy and on complete hormone supplementation, were investigated 34 years after diagnosis
- 17 CO-CP survivors (36 years (18-49 years) with complete hormone supplementation but without HT involvement according to peroperative neurosurgical assessment
- Comparisons were made to 27 age and sex matched controls regarding DTI parameters in the HT as well as for BMI, fat mass, fat free mass and waist/hip measurements

Results

DTI in hypothalamus in 29 ALL survivors and in 17 CO CP survivors compared to 27 healthy matched controls

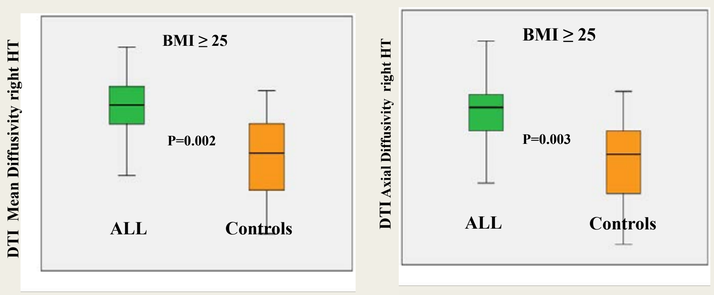
	ALL survivors (n=29) Median (range)	CP survivors (n=17) Median (range)	Controls (n=27) Median (range)	P ALL vs Controls	P CP vs Controls
Right hypothalamus					
Fractional anisotrophy	0.27 (0.20-0.34)	0.29 (0.19-0.35)	0.29 (0.25-0.35)	0.04	NS
Mean diffusivity	1.13 (0.89-1.24)	0.97 (0.85-1.10)	1.00 (0.77-1.21)	<0.001	NS
Axial diffusivity	1.41 (1.18-1.64)	1.21 (1.11-1.37)	1.25 (1.02-1.49)	<0.001	NS
Radial Diffusivity	0.99 (0.74-1.19)	0,85(0.72-0.99)	0.86 (0.65-1.07)	<0.001	NS
Left hypothalamus					
Fractional anisotrophy	0.30 (0.20-0.35)	0.32 (0.22-0.36)	0.31 (0.25-0.34)	NS	NS
Mean diffusivity	1.00 (0.76-1.08)	0.87 (0.72-1.01)	0.93 (0.78-1.12)	0.01	NS
Axial diffusivity	1.27 (0.97-1.37)	1.14 (0.97-1.31)	1.18 (1.01-1.39)	0.01	NS
Radial Diffusivity	0.87 (0.66-0.97)	0.73 (0.60-0.89)	0.79 (0.65-0.98)	0.01	NS

DTI in hypothalamus (HT) in ALL survivors (n=29) *vs* CP survivors (n=17) and control subjects (n=27)



No treatment is currently available for these hypothalamic problems
The mainstay is tailored healthy life-style support and proper hormone replacement

DTI in hypothalamus in ALL survivors with BMI ≥ 25 compared to control subjects with BMI ≥ 25



Metabolic risk markers and DTI in hypothalamus in 19 ALL survivors with BMI ≥ 25 compared to ALL survivors with BMI < 25

	ALL survivors BMI ≥ 25 N = 19	ALL survivors BMI < 25 N = 9	P
Age at diagnosis	4.4 (1.1-17)	3.2 (1.1-13)	NS
Height (cm)	1.61 (1.47-1.85)	1.73 (1.46-1.85)	NS
Weight (kg)	73.9 (55.9-123.5)	64,2 (38.7-74.8)	0.009
BMI (kg/m^2)	29 (25.2-39.1)	23.2 (18.2-24.9)	<0.001
Fatfree mass (kg)	41.2 (30.3-73)	45.8 (26-52.6)	NS
Fat mass (kg)	30.2 (14-55.3)	23.4 (10.6-30)	0.007
Glucose (mmol/L)	5.3 (4.1-13.6)	5.2 (4.9-6.5)	NS
Insulin (mIE/L)	11 (2-32)	11 (4-26)	NS
Leptin (µg/L)	29.5 (5.0-90.0)	13 (2.2-23)	0.01
Ghrelin (ng/L)	1145 (556-2400)	1140 (634-3670)	NS
Right hypothalamus			
Mean diffusivity	1.17 (0.97-1.34)	1.08 (0.89-1.77)	0.03
Axial diffusivity	1.44 (1.21-1.69)	1.37 (1.18-1.57)	0.02

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