Center for SUDEP Research: Morphometry Core/Pre-mortem Imaging: Preliminary Results

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Background: The causes of sudden unexplained death in epilepsy (SUDEP) are still unknown but the respiratory and cardiac symptoms observed in witnessed cases suggest that a breakdown of the central autonomic control system plays an important role. A pilot study (1) using quantitative image processing found evidence for brainstem damage in regions involved in autonomic control in the MRIs of two patients who later died of SUDEP that significantly exceeded the brainstem damage occasionally seen in other epilepsy patients. This indicates that it might be possible to use MRI to identify patients with a heightened risk for SUDEP. The purpose of the pre-mortem imaging project of CSR Morphometry Core is further investigate this possibility. This is done by obtaining and analyzing MRIs obtained for clinical purposes from patients who died of SUDEP. In contrast to MRIs acquired in research settings where all factors influencing quantitative image processing are strictly controlled, MRIs acquired in clinical settings are acquired on different MR platforms with different protocols and sequences. The second aim of this project is therefore to test to what degree quantitative analysis methods used in research settings can be used to process clinical data and to develop clinical imaging protocols suitable for quantitative imaging analysis and clinical needs.

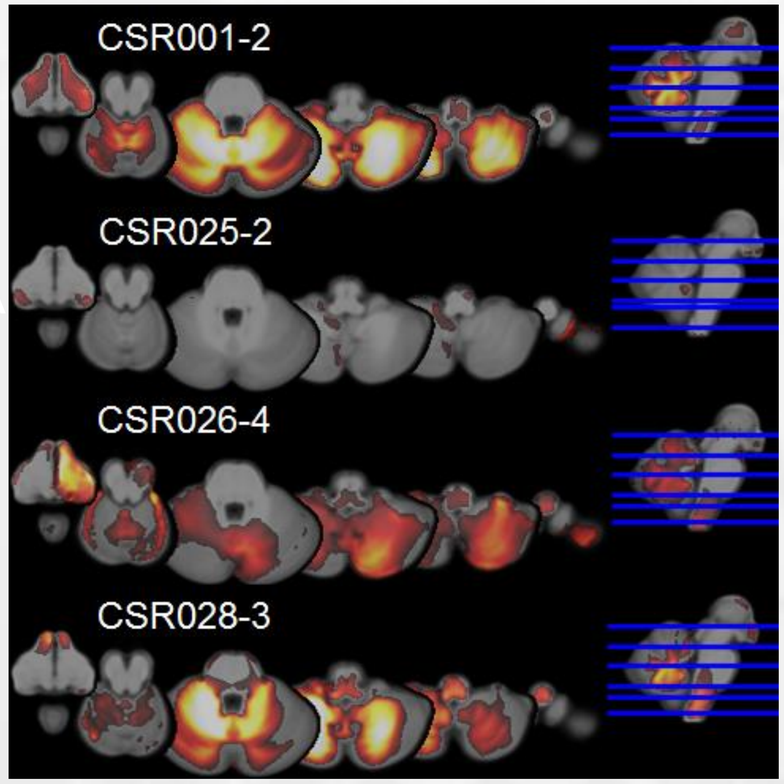
Methods: 24 whole brain T1 weighted images of 10 patients (mean age: 29.7±14.0, range 12 – 59 years) who died of SUDEP within 1-9 years after the last MRI (mean 3.3±2.2 years). 2 patients had several exams within a short period of time with allowing to assess the effects of different platforms, different field strength, sequences, contrast injection and noise on the detectability of brainstem lesions. Freesurfer was used generate a mask encompassing brainstem, cerebellum and thalamus/diencephalon for each that was used to extract the regions of interest.
The brainstem images were warped onto a brainstem atlas that had been generated from the MRIs of healthy controls who had undergone 3T MRI in a research setting with shot toolbox implemented in SPM12. The deformation matrices were used to calculate age and ICV adjusted z-score maps of the Jacobian determinants. The resulting maps were visually inspected for volume loss (z-score < -0.5) in the thalamus/diencephalon, at the level of the pontomesencephalic junction, mid pons, pontomedullary junction, medulla, lower medulla

Results: Please see Table 1 for findings in individual subjects. The cerebellar and thalamic atrophy follows the pattern commonly seen in epilepsy patients. Brainstem atrophy was found in all patients, most commonly in the ponto-mesencephalic junction followed by the medulla and ponto-medullary junction. Image noise (motion or accelerated acquisition), sequence type and field strength influenced the severity of the volume loss but not its distribution. Gadolinium injection not only changed the severity but also the distribution.

Table 1.

ID	years before SUDEP	cerebellum	thalamus	ponto-mesencephalic	mid pons	pontomedullary	medulla	lower medulla
CSR001-2	3	+	bilateral +	-	-	**+**	+	-
CSR011-1	2	+	bilateral +	**+**	+	+	+	+
CSR017-1	3	+	unilateral +	**+**	-	-	+	-
CSR022-2	3	+	bilateral +	(+)	(+)	**+**	(+)	-
CSR024-5	4	+	bilateral (+)	**+**	(+)	-	-	-
CSR025-2	3	+	bilateral +	-	-	-	**+**	-
CSR026-4	1	+	bilateral +	**+**	-	+	+	+
CSR028-3	2	+	bilateral +	-	+	**+**	+	+
CSR036-2	4	+	bilateral +	**+**	+	+	+	+
CSR039-2	9	+	bilateral +	**+**	+	+	+	+

- atrophy absent; + atrophy present; bold maximum atrophy



Conclusions: These preliminary findings suggest that it is possible to use MRI acquired for clinical purposes for quantitative image analysis. However, due to the different contrast to noise behavior of the different sequences, it is necessary to assess the atrophy pattern rather than to use absolute values as it is done in images acquired in research settings. The atrophy pattern found in this data set was similar than that found in the pilot study, i.e., the most prominent findings were in the tegmentum/ponto-mesencephalic junction and ponto-medullar junction that contain structures involved in autonomic control.

1. Mueller et al. Neuroimage Clin 2014;5:208-216

Supported by U01NS090406-02 to AMG