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VOLUMETRIC ANALYSIS OF HIPPOCAMPUS AND MEDIAL TEMPORAL LOBE IN BRAIN IN STRESS COMPACT AREA EXPOSURE

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ABSTRACT

This study used quantitative volumetric magnetic resonance imaging techniques to explore the neuroanatomic correlates of chronic, combat stress disorder in 30 young undergraduate Palestinian subjects whom suffering from continuous strong stress in their life spam as a result from *Israeli* occupation and compare their brain volumes with 30 young undergraduate British people whom doesn't suffering from any difficulty during their life. The first one-way ANOVA was conducted to check the differences in the volume of the hippocampus. There was a significant mean effect of the hippocampus volume ($F_{1.116}$=5.57, p=0.001), indicating that the mean volume of the hippocampus the British male group is significantly larger than the hippocampus volume in the second Palestinian male group this show that the prolonged stresses cause morphological changes in the size of the hippocampus with significant clinical effects. The effect of laterality (different between right and left hippocampus volume) was not significant (p=0.387 for British group; p= 0.368 for Palestinian group subject). There were no statistically significant group differences in medial temporal lobe and hemispheric brain volume. Study finding of decreased hippocampal volume in chronic stress subjects is consistent with results of other investigators which suggests that chronic stress may damage the hippocampus and this can be consider as risk factor for reduction hippocampus volume under the combat area exposure.

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INTRODUCTION

Measurement human brain volume been an important topic in Neuroscience for over a century. The last few decades have seen the increasing application of stereological methods - notably the Cavalieri method - to estimate brain volume using noninvasive imaging techniques (Mayhew and Olsen, 1991; McNulty *et al*., 2000; Garc#a-Finana *et al*., 2003). The stereological estimation of brain cortices or subcortical from Magnetic Resonance (MR) images. has been established as a research tool to investigate the volumetric change in the hippocampus and medial temporal lobe structures (Acer, 2008; Acer, 2009 Acer). Medial temporal lobes are an important part of the limbic system responsible for learning, memory, and emotion (Barense *et al*., 2005; Baxter, 2009), they consist of several inter-connected structures that include the temporal pole, Hippocampal Formation (HF) and the parahippocampal region (PHR). Among them, the HC is the most studied component of the MTL memory system and is a main contributor to the memory-related information acquisition and spatial navigation; Magnetic resonance (MR) imaging has been used in studies of the hippocampal formation and in amygdala biometric studies for several years. The biometric data are useful for evaluating selective hippocampal atrophy in patients with intractable partial seizures (Adler, 2014; Augustinack *et al*., 2014; Augustinack *et al*., 2013) 1–3), chronic stress and schizophrenia (Entis, 2012; Iglesias *et*

al., 2015; Sapolsky *et al*., 1983). Several studies from magnetic resonance imaging (MRI) studies have reported that patients diagnosed with posttraumatic stress disorder (PTSD) resulting from traumatic experiences such as military combat, sexual assault, or child abuse have a smaller hippocampus (up to 8% reduction) than comparably matched control subjects (Bremner *et al*., 2012; Bremner *et al*., 1999). The present study aims at finding both morphometrical and stereological estimates of the hippocampus volume, media temporal lobe and hemisphere brain volume MTL to investigate any significant difference in these volumes for British young male subjects whom have easy life compared with Palestinian young male subjects whom suffering from chronic stress life under Israeli occupation

MATERIALS AND METHODS

Subjects

30 young normal male undergraduate students of the University of Liverpool in United Kingdom (UK) universities and 30 young normal male undergraduate students of the Arab American university form Palestine Universities participated in this experiment. The average age of the first group subjects was 21.2 years and that of the second group subjects was 20.6 years. The mean age of the whole group was 21.0 years (range 18- 28**).** English was the first language for first group subjects while the Arabic language for second group the subjects, and none of them had ever suffered from any neurological or psychiatric problem. All the subjects had to pass a medical screening check that was carried out prior to scanning at the Magnetic Resonance and Image Analysis Research Centre (MARIARC) in the Faculty of Medicine at the University of Liverpool while Palestinian group had been checked at medical imaging department in An-Najah National University.

MR image acquisition and analysis procedure

The brains of the first group of 30 healthy male were scanned using a 3T Siemens TRIO whole body imaging system (Siemens Medical Solutions, Erlangen, Germany). In order to obtain good grey/white contrast, subjects were scanned using a T1-weighted MDEFT sequence (Deichmann *et al*., 2004). This sequence, which was adapted for the Liverpool scanner, had a TR of 7.92 ms, a TE of 2.48 ms and a flip angle of 16º. Slice thickness was 1 mm through the brain and the field of view was 25.6 cm. The images were acquired along the AC-PC line then these images were oriented perpendicularly to the long axis of the hippocampus and the voxels were isotropic and 1 mm in cross-section. The brain of second group of 30 healthy male were scanned at An-Najah Hospital University by 1.5 T Philips Ingenia whole body imaging system, subjects were scanned using a T1-weighted FFE sequence, this sequence had TR 400, TE 8.9ms, slice thickness 0.62 mm and pixel size in x-axis=0.48 mm and y-axis is= 0.48mm, the image for each subjects was acquired along the perpendicular axis of the hippocampus

Image processing

The volumes of the left and right hippocampus, temporal lobes and hemispheres were measured using image sections that were oriented perpendicularly to the long axis of the hippocampus (Jack *et al*., 1990; 1994; Ashtrati *et al*., 1991; Cook *et al*., 1992; Kuziencky and Jackson, 1995; Saitoh *et al*., 1995; Mackay *et al*., 1998). Therefore, for all the measurements, the image were acquired from image scanner were oriented perpendicular to the long axis of the hippocampus (Mackay and Roberts *et al*., 1998; Ding and Van Hoesen, 2015), Dalton *et al*, 2017) and also Berron *et al*, 2017) rather than perpendicular to the AC-PC line (anterior commissure-posterior commissure line) (Kate *et al*, 1997; Insausti and Juottonen *et al*., 1998). This orientation was used because many believe that the hippocampus (the structure of major interest) is best-visualized perpendicular to its long axis (Kuzniecky and Jackson, 1995; Rusch *et al*., 2001).

RESULTS

The results are reported in the following order: volumes of medial temporal lobe (MTL) , hippocampus volume and total hemispheric volume they been measured by stereology then they compared between the first group of UK male and second group Palestinian male subjects. Table 2 shows the means, SDs, CVs and ranges of right and left cerebral hemisphere, temporal lobe and hippocampus volume for first group 30 male and 30 second group male healthy subjects. A series of 3 one-way ANOVAs with a between subjects factor of (first group versus second subjects) and a within subjects factor of laterality (left versus right) was conducted in order to see whether there were laterality differences structure/region volumes. The first one-way ANOVA was conducted to check the differences in the volume of the hippocampus. There was a significant mean effect of the hippocampus volume ($F_{1.116}$=5.57, p=0.001), indicating that the mean volume of the hippocampus in the first British male group is significantly larger than the hippocampus volume in the second Palestinian male group. The effect of laterality (different between right and left hippocampus volume) was not significant (p=0.387 for British group; p= 0.368 for Palestinian group subject). The second the one -way ANOVA was conducted to check for groups differences in the volume of the temporal pole. There was a non-significant effect of temporal lobe volume in both group ($F_{1,116}$= 0.449 , p=0.718). There was no significant main effect of laterality (right and left temporal lobe volume) (p=0.254) and form Palestinian subjects (p=0.917). The last one-way ANOVA was conducted to check for sex differences

Table 1. Means, SDs, CVs and ranges of right and left absolute structure volumes for 30 British male subjects and 30 Palestinian healthy subjects with both group shown separately; SDs are shown in parentheses

Structure		British people			Palestinian people		
		Mean (SD)	CV	Range	Mean (SD)	CV	range
Hippocampus	R	2.88 (0.32)	11%	2.35-3.54	2.64 (0.29)	11%	2.03-3.29
	L	2.81 (0.38)	14%	2.11-3.48	2.58 (0.28)	11%	1.86-3.24
Temporal lobe	R	76.06 (9.5)	13%	50.4-93	68.32 (8.05)	12%	52.8-88.2
	L	78.36 (8.61)	11%	51-94.20	69.78 (8.46)	12%	52.8-88.2
Hemisphere	R	29.42 (6.21)	21%	17.44-41.55	24.74 (5.89)	24%	11.37-37.24
	L	598.22 (54.65)	9%	482.63-739.13	536.28 (44.3)	8%	462.38-637.88

in the volume of the cerebral hemispheres. There was a non-significant effect of brain hemispheres volume in both group ($F_{1.116}$=0. 889, p= 0.449), indicating that no significant different between the volume of the cerebral hemispheres in both group. The effect of laterality (right and left hemisphere of the brain volume) was not significant in both groups; in the British group p=0.624) and Palestinian group (p=0.728).

DISCUSSION

The results from this study that compare between Palestinian people whom suffering from continuous strong stress in their life spam as a result from *Israeli* occupation and compare their brain volumes with British people whom doesn't suffering from any difficulty during their life show that the prolonged stresses cause morphological changes in the size of the hippocampus with significant clinical effects. Human brain imaging studies have reported that people with a history of stress in their lives had a smaller hippocampal size, which is associated with differences in verbal memory. (Gilpertson *et al*., 2002) and these studies are crosspondant with our study finding , a study of magnetic resonance imaging in the last longitudinal mice showed that chronic stress restraint causes a decrease in the size of the hippocampus of the size of the stress (Lee *et al*., 2009). It is likely that these effects are mediated by the effects of stress on neuronal morphology and / or neurons in the hippocampus. The study found that there is a clear difference in the size of the hippocampus between Palestinian youth and their British counterparts, while there is no clear difference in the overall size of the brain. This can be explained by the fact that the lives of Palestinians living under occupation are subject to constant stress during their movements, their movement, their targeting and humiliation, and often to their arrest of terrorism, especially young people aged 16-26. They are the target group in this study, which leads to the suffering of this category of chronic stress and restraint reduces transient number of spine spasm, hierarchical branches of neurons in the CA3 (Conrad *et al*., 1999) and suppressing the production of neurons in the dentate falsifications (Schoenfeld and Gold, 2012) hippocampus areas. It seems that this structural change in the hippocampus after stress corresponds to the differences in spatial navigation and episodic memory resulting from stress (Kim Diamond, 2002; Vyas *et al*., 2002). This is observed significantly on the lives of everyday people and in some cases, the tendency of some young people to violence, confirms that some of the changes that which confirms that there are some changes that get the composition of the neural network in their brains. The limitation of this study did not take the body factors during it analysis which it may affects the results. Since there is no significant difference in the size of the hemispheric volume of the brains between two groups subjects in the same time British data did not take the body factor into the consideration. Therefore, the author believes that the effect of the body factor on the results was restricted. The future study the author recommended size of the samples had to be larger with regard to the body factors coefficient.

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