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Occipital bending (Yakovlevian torque) in bipolar depression

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ABSTRACT

Differing levels of occipital lobe asymmetry and enlarged lateral ventricles have been reported within patients with bipolar disorder (BD) compared with healthy controls, suggesting different rates of occipital bending (OB). This may exert pressure on subcortical structures, such as the hippocampus, reduced among psychiatric patients. We investigated OB prevalence in 35 patients with BD and 36 healthy controls, and ventricular and occipital volumes. Prevalence was four times higher among BD patients (12/35 [34.3%]) than in control subjects (3/36 [8.3%]), as well as larger lateral ventricular volumes (LVVs). Furthermore, we found OB to relate to left-to-right ventricular and occipital lobe volume (OLV) ratios. Those with OB also had reduced left-to-right hippocampal volume ratios. The results suggest that OB is more common among BD patients than healthy subjects, and prevalent in both BD Type I and Type II patients. We posit that anomalies in neural pruning or ventricular enlargement may precipitate OB, consequently resulting in one occipital lobe twisting around the other. Although the clinical implications of these results are unclear, the study suggests that asymmetrical ventricular volume matched with a pattern of oppositely asymmetrical occipital volume is related to OB and may be a marker of psychiatric illness.

1. Introduction

Bipolar disorder (BD) is a devastating mood disorder with up to 4–6% lifetime prevalence in adults (Johnson and Johnson, 2014). Various brain regions have been implicated in BD, including reduced total brain volume (TBV) (Bora et al., 2010), compromised white matter (WM) integrity (Liu et al., 2010), and altered blood flow (Vargas et al., 2013). Significant findings have been noted in the frontal, parietal, occipital and temporal lobes in those with BD Type I and Type II, including the hippocampus (Rimol et al., 2010, 2012; Foland-Ross et al., 2011; Elvsashagen et al., 2013; Liang et al., 2013). For example, Elvsashagen et al. (2013) reported significant thinning in BD patients in two prefrontal clusters primarily comprising the left subgenual anterior cingulate cortex, left perigenual ventromedial prefrontal cortex (PFC), bilateral dorsomedial PFC, and bilateral dorsolateral PFC, consistent with the findings of Foland-Ross et al. (2011). Liang et al. (2013) found normalized regional homogeneity in the right insular cortex, left middle frontal gyrus, left precuneus, left occipital lobe, left parietal, left superior frontal gyrus and left thalamus, as well as in the right anterior lobe of cerebellum, pons, right precentralgyrus, left postcentralgyrus, left inferior frontal gyrus, and right cingulate, in BD patients. Hippocampal volume reduction in BD patients has been reported in a number of studies (Kempton et al., 2011; Gao et al., 2013; MacMaster et al., 2014).

The phenomenon of a crossing of the interhemispheric fissure by one hemisphere into the domain of the other has been termed 'Yakovlevian torque', based on a 1966 article published by Yakovlev and Rakic (1966) or simply 'torque' by some investigators (Bilder et al., 1999; Toga and Thompson, 2003). The 'torquing' could be related to spatial displacement of the left and right hemispheres with respect to one another rather than to a difference in the amount of tissue in these regions (Watkins et al., 2001). This difference is even seen on a commonly used T1-weighted template (MNI305 template) to which raw scan data are often normalized; if there is rightwards (left around right) torquing, then this would result in more gray matter (GM) erroneously being assigned to the right hemisphere and a finding of rightwards asymmetry or an underestimate of leftward asymmetry (Amunts et al., 2000; Watkins et al., 2001).

Whilst there have been a number of studies reporting brain asymmetries in mood disorders (e.g., Barrick et al., 2005; Mackay

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et al., 2010; Maller et al., 2014), we previously examined occipital twisting (Maller et al., 2014), the occipital component of Yakovlevian torque, rather than volumetric asymmetry or lobar length. We (Maller et al., 2014) studied patients with major depression and reported occipital bending (OB) to be three times as prevalent among these patients when compared with matched controls. We define occipital bending (OB) to mean that one of the occipital lobes crosses the antero-posterior axis (Corballis and Morgan, 1978).

Differences in brain lateralization have been suggested in psychiatric disorders; hence a pattern of brain asymmetry may be a biomarker for these disorders. Some research suggests asymmetry may differ between individuals with schizophrenia and matched controls (Luchins et al., 1979; Luchins and Meltzer, 1983; Crow et al., 1998; Clark et al., 2010). A study by Deutsch et al. (2000) found that the anterior–posterior midline deviation scores in patients with schizophrenia were greater than in controls, with a higher prevalence of rightward OB (leftward asymmetry, indicating greater left hemispheric volume). In line with that finding, Zhao et al. (2009) reported 'interhemispheric fissure bending' along the sagittal plane to be significantly more prevalent in schizophrenia and the extent of OB to be greater in patients than in controls.

OB and occipital asymmetry have not been intensely investigated in affective disorders, although studies of altered hemispheric activity have been reported (e.g., Saletu et al., 2010; Oertel-Knochel and Linden, 2011; Hayashi et al., 2012). Additionally, total lateral ventricular volume (LVV) has been shown to be enlarged in BD patients (Arnone et al., 2009; Mackay et al., 2010; Rimol et al., 2010; Hallahan et al., 2011; Hartberg et al., 2011; De Peri et al., 2012; Jogia et al., 2012), which could possibly displace the occipital lobes laterally and posteriorly. Furthermore, if there is lateral ventricular asymmetry, it is possible that the hemisphere with greater cerebrospinal fluid volume (CSF) will twist around the other, as previously hypothesized (Maller et al., 2014). Fig. 1 illustrates this line of reasoning.

It is possible that OB may differentiate healthy controls from BD patients, and we are aware of no other studies that have assessed OB from magnetic resonance imaging (MRI) scans in this patient population. We hypothesized that OB prevalence would be greater in BD patients than in controls and that OB would be more rightwards than leftwards. Furthermore, we hypothesized that lateral ventricular volume would be greater among those with BD and greatest in those with OB, particularly on the side of occipital bending. That is, left ventricular volume was predicted to be greater than that on the right in that with rightwards OB.

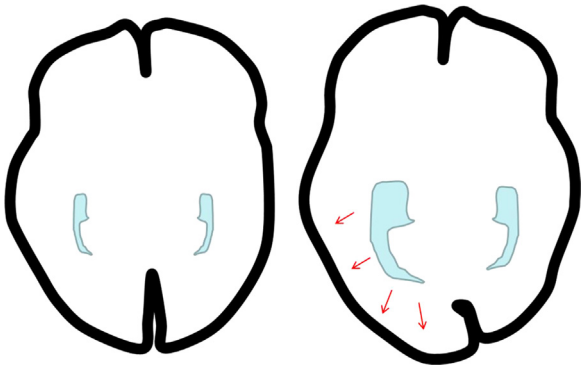

Fig. 1. A model of occipital lobe displacement due to enlarged lateral ventricles (blue) leading to occipital bending (OB). Red arrows denote the direction of occipital lobe displacement stemming from ventricular enlargement. Left: No ventricular enlargement or OB. Right: Ventricular enlargement with rightwards OB. Images are in neurological convention. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1
Descriptive statistics for bipolar disorder (BD) and control subjects.

Variable	Group	
	BD	Control
Number (M:F)	35 (14:21)	36 (17:19)
Years of age mean	45.71 ± 10.12	42.89 ± 12.60
HAMD mean	24.09 ± 4.1 range:17–33	N/A
Number of episodes	8.54 ± 6.26 range: 1–30	N/A
Total GM (L)*	0.604 ± 0.049	0.639 ± 0.065
Total WM (L)	0.452 ± 0.086	0.456 ± 0.130
CSF (L)	0.219 ± 0.109	0.176 ± 0.071
TBV (L)	1.171 ± 0.230	1.226 ± 0.154
ICV (L)	1.609 ± 0.183	1.604 ± 0.178
TBV/ICV	0.729 ± 0.121	0.772 ± 0.127
	Group	
	BD Type I	BD Type II
Number (M:F)	17 (5:12)	18 (9:9)
Years of age mean	43.12 ± 11.15	48.17 ± 8.64
HAMD mean (S.D.)	23.29 ± 4.15	24.83 ± 4.02
Number of medications	6.53 ± 5.90 range: 1–15	8.06 ± 5.58 range: 1–15
Number of episodes	9.41 ± 6.77 range: 1–30	7.72 ± 5.81 range: 1–15
Total GM (L)	0.606 ± 0.046	0.602 ± 0.053
Total WM (L)	0.472 ± 0.065	0.434 ± 0.101
CSF (L)	0.226 ± 0.065	0.213 ± 0.113
TBV (L)	1.127 ± 0.178	1.212 ± 0.269
ICV (L)	1.628 ± 0.149	1.591 ± 0.213
TBV/ICV	0.693 ± 0.088	0.764 ± 0.140

Note: ± =S.D.; CSF=cerebrospinal fluid; F=females; GM=gray matter; L=Litres; M=males; HAMD=Hamilton Depression Rating Scale; BD=bipolar disorder; N/A=not applicable; S.D.=standard deviation; WM=white matter; TBV=total brain volume; ICV=total intracranial volume. For total GM (L) between BD and controls, $F(1,69)=6.616$, $p=0.012$.

* $p < 0.05$.

2. Methods

2.1. Participants

The sample included 35 subjects with a diagnosis of BD (two left-handed, two ambidextrous, 31 right-handed; males=14) aged 29–69 years (mean age=45.71, S.D.=10.12; males mean=50.50, S.D.=10.23, females mean=42.52, S.D.=8.90) and 36 controls (all right-handed; males=17; mean age=42.89, S.D.=12.60; males mean age=41.18, S.D.=11.65, females mean age=43.42, S.D.=13.52). There were 17 subjects with BD Type I and 18 with BD Type II (Table 1). The mean number of medications tried within the BD group was 7.31 (S.D.=5.70) and the mean number of episodes was 8.54 (S.D.=6.26) with no significant differences between BD Type I and Type II patients. All BD patients were diagnosed according to DSM-IV criteria by a psychiatrist. Depression severity was measured with the Hamilton Depression Rating Scale (HAMD (Hamilton, 1960)). Handedness was determined by the Edinburgh Handedness Inventory (Oldfield, 1971). Participants were recruited either by public notice or word of mouth from the clinical services of The Alfred Hospital, Victoria, Australia. Exclusion criteria included axis I comorbidity except for the presence of generalized anxiety disorder or social phobia, current active medical problem, a known neurological disease or a contraindication to MRI scanning. Healthy control subjects were required to have no history of psychiatric illness. All subjects provided written informed consent on a form approved by the Alfred Human Subjects Research and Ethics Committee.

2.2. Magnetic resonance imaging

A 1.5T GE Signa Imaging System (General Electric Medical Systems, Milwaukee, WI) was used to acquire a contiguous sagittal IR-prepared SPoiled Gradient Recalled (SPGR) T1-weighted sequence for volumetric estimations (TR=8.628, TE=1.924, IT=300, matrix size 256 × 256, 0.94 mm × 0.94 mm, number of excitations=1, slice thickness=1.5 mm) for each subject.

All T1-weighted scans were viewed in MRIcro (http://www.mccauslandcenter.sc.edu/mricro/mricro/) from axial perspective and visually inspected for OB whereby one occipital pole extended across the midline (interhemispheric fissure), which refers to the narrow groove separating the left and right cerebral hemispheres and is identified from axial by looking for a large sulcus between the occipital poles; this is verified from the coronal orientation, which demonstrates a