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Review

Vestibular insights into cognition and psychiatry ☆

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ABSTRACT

The vestibular system has traditionally been thought of as a balance apparatus; however, accumulating research suggests an association between vestibular function and psychiatric and cognitive symptoms, even when balance is measurably unaffected. There are several brain regions that are implicated in both vestibular pathways and psychiatric disorders. The present review examines the anatomical associations between the vestibular system and various psychiatric disorders. Despite the lack of direct evidence for vestibular pathology in the key psychiatric disorders selected for this review, there is a substantial body of literature implicating the vestibular system in each of the selected psychiatric disorders. The second part of this review provides complimentary evidence showing the link between vestibular dysfunction and vestibular stimulation upon cognitive and psychiatric symptoms. In summary, emerging research suggests the vestibular system can be considered a potential window for exploring brain function beyond that of maintenance of balance, and into areas of cognitive, affective and psychiatric symptomology. Given the paucity of biological and diagnostic markers in psychiatry, novel avenues to explore brain function in psychiatric disorders are of particular interest and warrant further exploration.

Contents

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1. Introduction

The vestibular system has traditionally been thought of as a balance apparatus that is related to brain disorders only when co-morbid symptoms include balance compromise, such as in Meniere's disease and Parkinson's disease. However, accumulating research suggests an association between vestibular function and psychiatric disorders, even when balance is apparently unaffected. Recent research has described the vestibular system as a potential window for exploring brain function beyond that of maintenance of balance, and into areas of perception, cognition, and consciousness (Lopez and Blanke, 2011). Existing research describes clear links between symptoms of anxiety and depression and the vestibular apparatus, and there is some preliminary evidence suggesting a link between the vestibular system and symptoms of psychosis and mania. Aspects of cognition, particularly spatial memory and spatial perception, have also been linked to vestibular function. The two key anatomical regions that provide links between the vestibular system and neural networks involved in cognitive and emotional processing are the parabrachial nucleus and the hippocampus (Balaban and Thayer, 2001; Balaban et al., 2002; Balaban, 2004a); however, many of the neuroanatomical regions that are linked to the vestibular system are also implicated in several psychiatric illnesses. The past decade has seen an increased interest in the relationship between the vestibular system and mood, cognition and psychiatric symptoms with studies demonstrating vestibular stimulation can produce changes in mood, cognition and psychiatric symptoms (Dodson, 2004; Levine et al., 2012; Winter et al., 2012). Hence, the time is now ripe to review the literature in an attempt to draw some overall conclusions. This review will firstly provide an overview of vestibular related brain structures that overlap with psychiatric disorders and then present a summary of how these regions of interest are implicated in prominent psychiatric disorder. The second section of the review will explore the cognitive and psychiatric symptoms that have been associated with vestibular (dys)function. Finally, we will bring these foci together to produce an overall summation of our current state of understanding of the relationship between vestibular function, psychiatric disorders, and cognition.

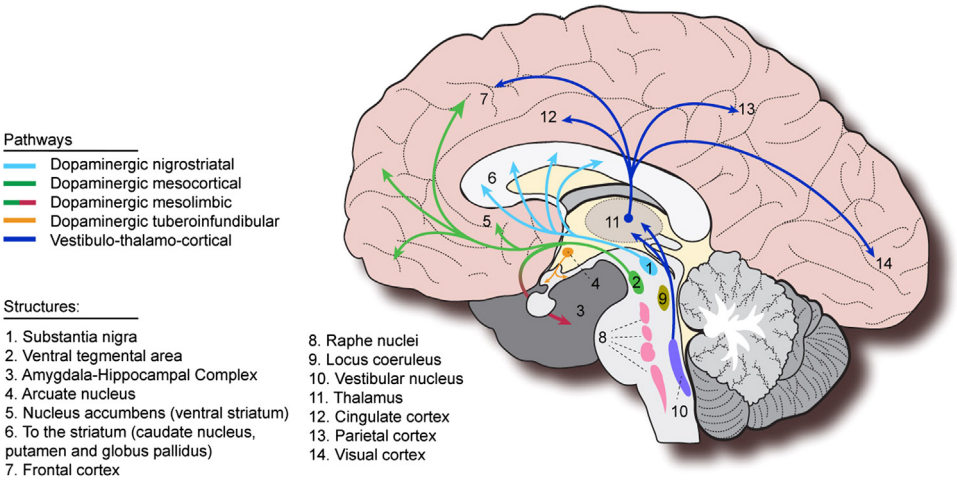
2. The vestibular system as a "Window to the Brain" for psychiatric symptoms

The vestibular system is vestigial and therefore intimately integrated into our central nervous system. Compromising a complex network of diverse pathways, there are vestibular origins within subcortical structures that traverse through the midbrain and then into the inner ear. With such diffuse connectivity, it is likely that vestibular function will be impacted upon at various stages of its pathways. Furthermore, it is comprised of both white matter and nerves, particularly the 8th cranial nerve (vestibulo-cochlear, which is a composite sensory nerve) hence vulnerable to different types of insults and/or compromised cell signalling. As illustrated in Fig. 1, neuroanatomical models of the vestibular system established through a variety of techniques including conventional and advanced structural MRI (e.g. T1-weighted and DTI), functional imaging (e.g. fMRI, magnetoencephalography (MEG)) and brain stimulation studies (e.g. galvanic or caloric vestibular stimulation; (Balaban and Jacob, 2001; Balaban et al., 2011; Bottini et al., 1994, 1995, 2001; Dieterich and Brandt, 2008; Emri et al., 2003; JA., 2004; Jones et al., 2009; Kisely et al., 2000, 2002; Rochefort et al., 2013; Tuohimaa et al., 1983; Vitte et al., 1996; Wenzel et al., 1996) indicate that vestibular signals travel from the vestibular nuclei to brain stem nuclei, then project to subcortical structures, and regions well-known to be related to balance and muscle-coordination, such as the cerebellum, and those central to vision (specifically the occipital lobe) as well as direct and indirect projections to several cortical regions.

Whilst there is no direct evidence to suggest direct pathology of the vestibular apparatus in psychiatric disorders, there are many well identified links between the vestibular system and brain regions implicated in cognitive and emotion processing, which provide a potential neurological basis for the coexistence of vestibular and psychiatric symptoms (Balaban and Jacob, 2001; Yardley et al., 1999).

2.1. *Brainstem links to the vestibular system*

In terms of brainstem regions, the raphe nuclei and locus coeruleus are both implicated in several psychiatric conditions as well as having reciprocal connections with the vestibular



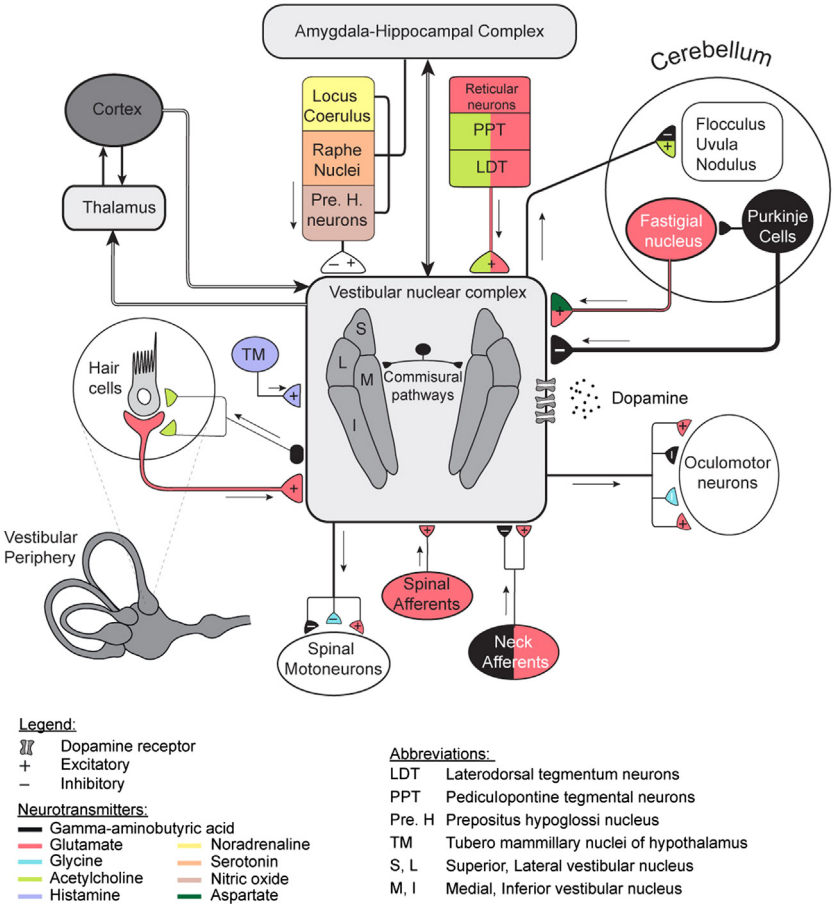


Fig. 1 – (a) and (b) A neuroanatomical model of the vestibular system.

nuclei. The *raphe nuclei* receives projections from the vestibular nuclei (Cuccurazzu and Halberstadt, 2008) and sends serotonergic and nonserotonergic projections to the vestibular nuclei (Halberstadt and Balaban, 2006; Kalen et al., 1985) as well as sending axon collaterals to the central amygdaloid nucleus, suggesting co-modulation of vestibular pathways with regions involved in affective control (Halberstadt and Balaban, 2006). The raphe-vestibular projections are organised into anatomically distinct fields which is thought to selectively modulate processing in regions of the vestibular nuclear complex that receive input from specific cerebellar zones, representing a potential mechanism whereby motor activity and

Table 1 – Examples of peer-reviewed publications supporting the relationship between regions of interest (ROI) implicated in the vestibular system and common psychiatric conditions. PD=Parkinson's disease; MDD=major depressive disorder; BPAD=bipolar affective disorder; SCZ=schizophrenia; BDD/OCD=body dysmorphic disorder/obsessive compulsive disorder; PTSD=post-traumatic stress disorder; ADHD=attention deficit hyperactivity disorder.

ROI	PD	MDD	BPAD	SCZ	BDD/OCD	PTSD	ADHD
Hippocampus (HC)	Beyer et al. (2013), Bohnen et al. (2008), Ibarretxe-Bilbao et al. (2011)	Maller et al. (2007, 2012a), Malykhin et al. (2012)	Hajek et al. (2012), Rossi et al. (2012)	Kusljic and Van Den Buuse (2012), Sanderson et al. (2012)	van den Heuvel et al. (2005)	Kozlovsky et al. (2012), Thomaes et al. (2010)	Geurts et al. (2012), Xia et al. (2012)
Raphe nuclei (RN)	Doty (2012), Mehnert et al. (2010), Pelled et al. (2007)	Bach and Arango (2012), Matthews and Harrison (2012)	Krogias et al. (2011), Matthews and Harrison (2012)	Kusljic and Van Den Buuse (2012), Matthews and Harrison (2012)	Graeff (1997), Harsanyi et al. (2007)	Luo et al. (2011), Sullivan et al. (2013)	Jucaite et al. (2005), Trinh et al. (2003)
Locus Coeruleus (LC)	Del Tredici and Braak (2012), Ohtsuka et al. (2013)	Arnold et al. (2012), Chandley et al. (2012), Lee et al. (2011), Ordway et al. (2012), Schrader et al. (2011), Zhu et al. (1999)	Baumann and Bogerts (2001), Bernard et al. (2011), Seager et al. (2005), Wiste et al. (2008)	Karson et al. (1991), Marner et al. (2005), Sasaki et al. (2008), Shibata et al. (2008)	George et al. (2008), Hashemi et al. (2007)	Adamec et al. (2012), Bracha et al. (2005), O′ Donnell et al. (2004)	Hegerl and Hensch (2012), Jones and Hess (2003), Kuwahata et al. (2002)
Thalamus (TH)	Halliday (2009), Planetta et al. (2013)	Diener et al. (2012), Sexton et al. (2013), Zeng et al. (2012)	Chen et al. (2012), Kraguljac et al. (2012)	Kraguljac et al. (2012), Parnaudeau et al. (2013)	Atmaca et al. (2010), Radua and Mataix-Cols (2009), Zuo et al. (2013)	Nikolaus et al. (2010), Shucard et al. (2012), Yin et al. (2011)	Geurts et al. (2012), Mills et al. (2012), Xia et al. (2012)
Amygdala (AG)	Baba et al. (2011), Dickson et al. (2010)	Lorenzetti et al. (2010), Malykhin et al. (2012), Stuhrmann et al. (2012)	Brown et al. (2011), Foland-Ross et al. (2012a, 2012b), Mahon et al. (2012)	Brown et al. (2011), Sara (2009)	Atmaca et al. (2008), Feusner et al. (2009), Szeszko et al. (1999)	Ding et al. (2013), Morey et al. (2012), Rabinak et al. (2011), Sripada et al. (2012)	Bitter et al. (2011), Frodl and Skokauskas (2012), Trinh et al. (2003)
Insular cortex (IC)	Lee et al. (2013a), Song et al. (2011b)	Diener et al. (2012), Lee et al. (2011), Sliz and Hayley (2012), Takahashi et al. (2010)	Delvecchio et al. (2012), Hummer et al. (2013)	Kasai et al. (2003), Takahashi et al. (2004)	Fan et al. (2013), Nakamae et al. (2012), Nishida et al. (2011), Song et al. (2011a)	Herringa et al. (2012), Morey et al. (2012)	Konrad et al. (2006), Lopez-Larson et al. (2012), Schneider et al. (2010)

Table 1 (*continued*)

ROI	PD	MDD	BPAD	SCZ	BDD/OCD	PTSD	ADHD
Anterior cingulate cortex (ACC)	Jokinen et al. (2013), Lewis et al. (2012)	Diener et al. (2012), Sacher et al. (2012)	Bertocci et al. (2012), Lim et al. (2013)	Holroyd et al. (2004), Premkumar et al. (2010)	Kuhn et al. (2012), Nishida et al. (2011), Pittenger et al. (2006)	Hayes et al. (2012), Kuhn and Gallinat (2013), Sartory et al. (2013)	Hart et al. (2013), Maier et al. (2013), Sun et al. (2012)
Prefrontal cortex (PFC)	Rae et al. (2012), Wang et al. (2012)	Fitzgerald et al. (2006), Sacher et al. (2012), Salerian and Altar (2012)	Lim et al. (2013), Townsend and Altshuler (2012), Van Rheenen and Rossell (2012)	Karbasforoushan and Woodward (2012), Kraguljac et al. (2012), Szeszko et al. (2005)	Feusner et al. (2008, 2009, 2010, 2011)	Ahmed et al. (2012), Qin et al. (2012), Shin et al. (2006)	Ramos-Quiroga et al. (2013), Tsujimoto et al. (2013)
Cerebellum (CR)	Bostan and Strick (2010), Nicoletti et al. (2006)	Baldacara et al. (2008), Ma et al. (2013), Peng et al. (2013), Yucel et al. (2012), Zeng et al. (2012)	Baldacara et al. (2008, 2011b), Liu et al. (2012a, 2013)	Baldacara et al. (2008), Freitag et al. (2013), Rigucci et al. (2012)	Hou et al. (2012), Palma et al. (2012), Tobe et al. (2010), Zarei et al. (2011)	Baldacara et al. (2011a), Bing et al. (2013), Morey et al. (2012)	Baldacara et al. (2008), Poissant et al. (2012), van Ewijk et al. (2012)
Occipital (OC)	Kostic et al. (2012), Tessitore et al. (2012a)	Liao et al. (2013), Peng et al. (2011), Seidman et al. (2011), Zeng et al. (2012)	Bellani et al. (2012), Bruno et al. (2008), James et al. (2011)	Boos et al. (2013), Lee et al. (2013b), Rigucci et al. (2012)	Arienzo et al. (2013), Buchanan et al. (2013), Feusner et al. (2010, 2013), Yaryura-Tobias et al. (2002)	Chao et al. (2012), Engdahl et al. (2010), Kroes et al. (2011), Tavanti et al. (2012), Whalley et al. (2013)	Gonzalez et al. (2013), Massat et al. (2012), Mazaheri et al. (2010), Nagel et al. (2011), Nazari et al. (2010)
Putamen (PU)	Brooks (2010), Halliday (2009), Sioka et al. (2010)	Amsterdam et al. (2012), Marchand et al. (2012), Sexton et al. (2013), Zeng et al. (2012)	Caseras et al. (2013), Chen et al. (2011, 2012), Hummer et al. (2013)	Chemerinski et al. (2013), Dougherty et al. (2012), Levitt et al. (2012, 2013)	Ahmed et al. (2012), Alvarenga et al. (2012), Harrison et al. (2009), Marsh et al. (2013), Moresco et al. (2007)	Filipovic et al. (2011), Linnman et al. (2011), Mickleborough et al. (2011), Nardo et al. (2011)	Frodl and Skokauskas (2012), Kim et al. (2010), Seidman et al. (2011)
Parietal lobe	Hayashi et al. (2009), Segura et al. (2013) Tessitore et al. (2012b)	Maller et al. (2012b), Orosz et al. (2012), Zuo et al. (2012)	Cui et al. (2011), Lin et al. (2011) Liu et al. (2012b)	Chen et al. (2013), Cui et al. (2011) Palaniyappan and Liddle (2012)	Feusner et al. (2008), Koprivova et al. (2009), Lazaro et al. (2009, 2011), Velikova et al. (2010)	Kroes et al. (2011, Landre et al. (2012), Metzger et al. (2004)	Cherkasova and Hechtman (2009), Hale et al. (2010), Silk et al. (2009)

Note: Schrader et al. (2011); trigeminal nerve stimulation.

behavioural arousal could influence the activity of cerebello-vestibular circuits (Halberstadt and Balaban, 2003). The *locus coeruleus* provides noradrenergic innervation to the vestibular nuclei (Schuerger and Balaban, 1999), as well as collateral projections to regions including the cerebellum, neocortex and hypothalamus, which have been hypothesised to mediate effects of arousal on vestibular reflex performance. The locus coeruleus also responds to vestibular stimulation (Manzoni et al., 1989) via direct projections from the vestibular nuclei (Balaban, 1996) and input from vestibular related sources (Luppi et al., 1995).

2.2. *Limbic regions, parabrachial nucleus and the vestibular system*

The limbic system is central to both vestibular function and emotional processing. The *parabrachial nucleus (PBN)* network provides a direct link between the vestibular system and neural networks involved in emotional processing. The PBN has reciprocal connections with the vestibular nuclei (Balaban and Thayer, 2001; Balaban, 2002, 2004b), as well as reciprocal connections with the amygdala, hypothalamus, locus coeruleus, and prefrontal cortex (Balaban and Thayer, 2001; Gorman et al., 2000; Schuerger and Balaban, 1999). The *amygdala*, *hypothalamus*, *locus coeruleus* and *prefrontal cortex* are all areas of the brain that are commonly linked with mental illnesses such as schizophrenia, bipolar disorder and depression (e.g. Bennett, 2011; Brown et al., 2011). The *hippocampus* is consistently implicated in cognition and models of psychiatric disorders and there is a large body of evidence supporting vestibular–hippocampal interactions (e.g. Besnard et al., 2012; Brandt et al., 2005; Hufner et al., 2007; Sharp et al., 1995; Smith et al., 2005a).

2.3. *Cortical connections to the vestibular system*

The exact locations and functions of cortical regions that process vestibular information remains unclear (zu Eulenburg et al., 2012). The *anterior cingulate cortex* has been considered part of the human vestibular cortex (Bottini et al., 1995, 2001; Lopez and Blanke, 2011; Lopez-Larson et al., 2012), hence it has been conceptualised that the anterior cingulate cortex may provide a bridge between the vestibular sensorimotor areas and the affect divisions of the prefrontal regions that entail motivational states (Bush et al., 2000). The *insular cortex* is one of the main cortical regions that receives information from the vestibular nuclei in the brain stem (Akbarian et al., 1994). The *prefrontal cortex* regions indirectly, by way of motor association cortices and anterior cingulate cortex, exert regulatory influence over the vestibular sensory areas for attenuation of sensory stimulation (Carmona et al., 2009). The *parietal cortex*, particular the parietal opercular area has been implicated as a core cortical region for vestibular processing (zu Eulenburg et al., 2012).

2.4. *Neurochemical influences on the vestibular systems*

In addition to the neuroanatomical links, the vestibular system is implicated in both the serotonergic and dopaminergic systems, which are key neurotransmitter pathways involved in psychiatric disorders. Vestibular nucleus neurons respond to stimulation of the dorsal raphe nucleus (a key source of serotonergic input), as well as exogenous serotonin (Licata et al., 1995) and a rise in serotonin levels is observed in the medial vestibular nuclei following vestibular stimulation (i.e. caloric stimulation) (Halberstadt and Balaban, 2006). Selective serotonin reuptake inhibitors (SSRIs) are efficacious in the treatment of vertigo (Johnson, 1998) and SSRI withdrawal is associated with vestibular manifestations (i.e. dizziness) (Coupland et al., 1996). In relation to dopamine, dopamine (D2) receptors have been identified in neurons of the medial vestibular nucleus and the lateral vestibular nuclei (Smith and Darlington, 1994) and meaningful levels of dopamine have been detected in a region of the vestibular nuclei (Cransac et al., 1996). There is also evidence to suggest that dopamine might exert a modulatory action on the vestibular system, either by a direct action on the vestibular neurons or by modulation of GABAergic transmission (Vibert et al., 1995). In vestibular-compromised rats (following hemi-labyrinthectomy), treatment with a D2 agonist (bromocriptine) accelerates compensation of postural and ocular symptoms, whereas treatment with a D2 antagonist (sulpiride) slows down recovery, suggesting dopamine plays a role in the recovery from vestibular asymmetries (Petrosini and Dell'Anna, 1993).

3. Vestibular related brain regions and psychiatric conditions

On the basis of the mini-review above, 12 vestibular related brain regions (region of interest; ROI) known to be related to psychiatric conditions were selected: raphe nuclei, locus coreuleus, hippocampus, amygdala, insular cortex, anterior cingulate cortex, putamen, prefrontal cortex, parietal lobe, occipital lobe, and cerebellum. These ROIs were based upon a model of pathways involved in psychiatric and vestibular symptoms reviewed above. A MedLine search was conducted whereby imaging and electrophysiological peer-reviewed publications supporting the association of each ROI to a psychiatric condition were included. The psychiatric conditions included: Parkinson's disease (PD), major depressive disorder (MDD), bipolar disorder (BPD), schizophrenia (SCZ), post-traumatic stress disorder (PTSD), body dysmorphic disorder (BDD) or obsessive compulsive disorder (OCD), and attention deficit hyperactivity disorder (ADHD). It was not our intention to find every publication that matched our criteria, but rather, to reference a small collection of studies, meta-analyses or review papers (if available), to demonstrate that the relationship has been supported (Table 1).

Whilst there is no evidence of specific vestibular pathology underlying any of the psychiatric disorders reviewed, Table 1 demonstrates that each of the major ROIs known to be related to vestibular apparatus are also significantly associated with key psychiatric disorders. Furthermore, some conditions have been found to have unique ROI variation which not only separates them from control (non-psychiatric) subjects, but each condition from one other. Hence, it is possible that vestibular function is related to not only psychiatric disorders per se, but measures of vestibular function could potentially

provide an avenue for discriminating between specific types of psychiatric disorders.

4. Cognitive and psychiatric symptoms associated with vestibular (dys)function

The second section of this literature review addresses what is currently known about cognitive and psychiatric symptoms associated with vestibular dysfunction. A MedLine/pubmed search was conducted that included the following key search terms 'vestibular'; 'cognition'; 'attention'; 'memory'; 'psychosis'; 'anxiety'; 'depression' and 'psychiatric'. Relevant articles were divided into those that explored the relationship between vestibular dysfunction and cognition and those that explored vestibular dysfunction and psychiatric symptoms.

4.1. *Vestibular dysfunction and cognition*

It has been well reported that patients with vestibular dysfunction experience impairments in postural control and gait; balance problems; ocular motor changes; dizziness and other behavioural changes including anxiety (Balaban, 2002; Cohen and Kimball, 2008; Mamoto et al., 2002; Schubert and Minor, 2004; Talkowski et al., 2005). Over the past decade, there has also been an increasing number of reports linking vestibular dysfunction with navigational and spatial memory impairments (Brandt et al., 2005; Schautzer et al., 2003; Smith et al., 2010), as well as a limited number of studies that suggest vestibular dysfunction may be linked to broader cognitive, psychiatric and behavioural changes (e.g. Caixeta et al., 2012; Grimm et al., 1989).

The historical context of the link between spatial memory and vestibular function comes from animal studies on spatial navigation that suggest that animals use vestibular cues to establish spatial maps of their environment and navigate their way through a familiar environment (see reviews (Etienne and Jeffery, 2004; Smith et al., 2005a; Stackman et al., 2002; Taube et al., 1996)). Vestibular lesioned rats demonstrate impairments in spatial learning (Ossenkopp and Hargreaves, 1993) and spatial navigation in the absence of visual cues (Stackman and Herbert, 2002). The spatial memory and navigation deficits are unlikely to be attributable to motor impairment (Stackman et al., 2002) or anxiety (Machado et al., 2012; Smith et al., 2010) and have also been described as long term or permanent deficits (Baek et al., 2010; Zheng et al., 2009b). There are also limited reports to suggest that cognitive deficits following bilateral vestibular deafferentation in rats extend beyond spatial memory, with reports of deficits in object recognition memory (Zheng et al., 2004), and attention (using a 5-choice serial reaction time task (Zheng et al., 2009a)).

The first human clinical paper to link vestibular dysfunction to cognition impairment (Grimm et al., 1989) reported on 102 patients with perilymph fistular syndrome (a rupture in the labrynth, resulting in leakage of perilymphatic fluid) who experienced vestibular symptoms (e.g. vertigo), as well as a range of cognitive and emotional symptoms. Results suggested that while these patients demonstrated a normal level of global intellectual functioning, their performance on several areas of cognition was impaired. This included psychomotor speed (digit symbol), visual construction abilities (block design), verbal learning (paired associate learning) and visual sequencing (picture arrangement). Since this initial report, there have been several human studies in patients with differing levels of vestibular loss that have reported deficits in path navigation, spatial memory, spatial perception and attention (Brandt et al., 2005; Caixeta et al., 2012; Cohen, 2000; Grabherr et al., 2011; Guidetti et al., 2008; Peruch et al., 1999; Schautzer et al., 2003).

4.1.1. *Bilateral vestibular loss and spatial memory*

Spatial memory deficits have been reported in a series of studies assessing patients with bilateral vestibular loss due to neurofibromatosis type 2 after bilateral vestibular neurectomy as compared to age- and sex-matched controls on a human adaptation of the Morris water task, a spatial navigation/maze task initially designed for rat experiments (Brandt et al., 2005; Schautzer et al., 2003). Results in 12 patients, compared to 10 healthy controls showed impaired performance when patients were required to recall a navigation path in the absence of a visible target. Furthermore, Brandt et al., (2005) demonstrated that patients were able to perform this task successfully if they were provided with a visible target and also noted that other aspects of memory (using the Wecshler memory scale) were intact, indicating that bilateral vestibular loss is specifically related to a deficit in spatial memory.

4.1.2. *Unilateral vestibular loss and spatial memory*

Findings of cognitive changes in unilateral vestibular loss have been less consistent. In a large study, 50 patients with unilateral labyrinthine hypofunction as a consequence of previous vestibular neuritis were compared to 50 age- and sex-matched healthy controls on their spatial working memory performance (using the Corsi block task) and their navigation abilities (Guidetti et al., 2008). Results showed spatial working memory as well as navigational impairments in both left and right labyrinthine-deficient patients as compared to controls. In contrast, an earlier study found a trend toward spatial memory and navigation impairments in patients with right, but not left, unilateral vestibular deafferentation (Hufner et al., 2007). Attention processes (involved in simple, inhibitory, and forced choice reaction time tasks) have also been described as compromised in patients with well compensated (no symptoms of dizziness or definable postural deficit) surgically confirmed unilateral vestibular loss, particularly when patients were simultaneously engaged in a postural challenge task (Redfern et al., 2004).

4.1.3. *Vestibular loss and stimulation: Spatial memory and beyond*

Beyond spatial navigation and memory, the capacity to perform mental rotation tasks has been reported as impaired in a small sample of patients ($n=8$) with bilateral vestibular loss as compared to 14 healthy controls (Grabherr et al., 2011). There is also some references in the literature associating vestibular loss with impairments with mental arithmetic or dyscalculia (Risey and Briner, 1990; Smith, 2012); however the findings are inconsistent (e.g. see Andersson et al. (2003)).

Some further support for vestibular input to various cognitive tasks is derived from galvanic and caloric vestibular stimulation studies. For example, a recent study applied suprathreshold bilateral bipolar galvanic vestibular stimulation to 120 healthy adults and compared their performance on a cognitive battery to a control condition which involved no GVS or subthreshold stimulation (Dilda et al., 2012). Results were consistent with the literature on bilateral vestibular loss and indicated that galvanic vestibular stimulation significantly degraded performance on short-term spatial memory, egocentric mental rotation (perspective taking) with no difference noted in other areas of cognition (including reaction time and dual tasking). An earlier study using unilateral caloric stimulation in healthy individuals suggested that caloric stimulation selectively activates contralateral cerebral structures and enhances cognitive processes mediated by these structures, with left ear stimulation improving spatial memory and right ear stimulation improving verbal memory (Bachtold et al., 2001).

Given that the cognitive changes in spatial memory associated with vestibular loss remain apparent 5–10 years following vestibular neurectomies (Brandt et al., 2005; Schautzer et al., 2003) and given that the spatial memory impairments persist when vertigo symptoms have subsided (Guidetti et al., 2008), it appears unlikely that the cognitive changes are simply a consequence or byproduct of other vestibular symptoms (such as ocular motor or postural symptoms). Rather, it is has been suggested that the strong anatomical links between the vestibular system and hippocampus underpin the behavioural link between the vestibular system and memory (reviewed by Smith et al., 2005b).

The central role of the hippocampus in spatial memory has been well documented (Epstein and Kanwisher, 1998; Maguire et al., 1997). Vestibular input to the hippocampus appears critical for spatial navigation and for updating brain representations of spatial information (Smith et al., 2005b; Stackman et al., 2002). There is considerable neuroanatomical and neurophysiological support for vestibular–hippocampal interactions (see Hufner et al., 2007; Lopez and Blanke, 2011; Smith, 1997); however the anatomical pathways connecting the vestibular system to the hippocampus are less clear and various vestibular–hippocampal pathways have been proposed, which are likely to involve the thalamus (see Lopez and Blanke, 2011; Smith, 1997). A neuroimaging study in 10 patients who had received bilateral vestibular nerve section 5–10 years before the test and subsequently had a complete acquired chronic bilateral vestibular loss exhibited a significant, selective bilateral atrophy of the hippocampus (16.9% decrease relative to controls), that was correlated with spatial memory deficits (Brandt et al., 2005). In contrast, patients with unilateral vestibular neurectomy did not demonstrate such hippocampal atrophy (Hufner et al., 2007), suggesting the vestibular input from one intact labyrinth appears to be sufficient to maintain the gross volume of the hippocampus in humans.

In sum, evidence derived from animal and human studies suggest that vestibular loss can lead to spatial memory and spatial navigational impairments which appear to be attributed to the anatomical links between the vestibular system and the hippocampus.

4.2. *Vestibular dysfunction and psychiatric symptoms*

Links between anxiety/panic and dizziness/vertigo have been described in medical literature since ancient times (see Balaban and Jacob, 2001 for a historical review). The link appears to be a complex, two-way interaction whereby people with anxiety, depression and other psychiatric symptoms commonly report vestibular symptoms (such as dizziness), conversely, people with vestibular dysfunction can experience a range of psychiatric/affective symptoms, predominantly anxiety, agoraphobia and depression (e.g. Balaban and Jacob, 2001; Balaban and Thayer, 2001; Eckhardt-Henn et al., 2008; Godemann et al., 2004; Pollak et al., 2003). It remains uncertain whether the psychiatric symptoms are a "reaction" to the distress of living with a vestibular disease or whether they represent alterations to the neural circuitry that involves anatomical and neurochemical (predominantly monoaminergic) connections between the vestibular system and areas such as the hippocampus, amygdala, and infralimbic cortex (Balaban, 2002) (as reviewed in the first part of this manuscript). It has also been suggested that because the vestibular system plays a role in controlling autonomic functions (e.g. heart rate, blood pressure) (Yates and Miller, 1998), alterations to these autonomic functions may also trigger a range of changes in cognition, emotion and personality.

4.2.1. *Vestibular dysfunction and affective symptoms*

There are several reports that suggest patients with vestibular disturbance experience symptoms of depression, anxiety and agoraphobia at higher rates than the general population (Eagger et al., 1992; Gazzola et al., 2009; Guidetti et al., 2008). In a study of 93 patients with objective evidence of peripheral vestibular disorder two thirds of the patients reported symptoms of depression and/or anxiety since the onset of the vestibular symptoms. Fifty-four of these patients were seen 3 to 5 years after their original referral and more than half the group (37 out of 54) were rated above the cut off point for significant psychiatric disturbance when interviewed. Panic disorder with or without agoraphobia and major depression were the commonest psychiatric diagnoses. There is some evidence to suggest that these symptoms are more than a reaction to the symptoms of vestibular dysfunction (e.g. vertigo or dizziness). For example, Guidetti et al., (2008) reported significantly higher levels of anxiety and depression in 50 patients with well compensated (no vertigo symptoms) unilateral labyrinthine hypofunction as a consequence of previous vestibular neuritis as compared to 50 age- and sex-matched healthy controls. Somewhat contrasting these findings is a recent prospective study that looked at predictors of anxiety (STAI) and depression (BDI) in 407 patients who presented with dizziness and vestibular disease (194 patients were diagnosed with BPPV, 75 with vestibular neuritis, 63 with Ménière's disease, 58 with migrainous vertigo, and 17 with presbystasis). Results suggested that rather than the type of vestibular disease, the best predictor of depression and anxiety was the patient's level of distress associated with symptoms of dizziness or vertigo (dizziness handicap inventory scores) (Hong et al., 2013).

A series of prospective, interdisciplinary studies were conducted to explore the relationship between comorbid

psychiatric disorders and symptoms in patients with various organic vertigo syndromes (Best et al., 2006; Eckhardt-Henn et al., 2008). Patients with organic vertigo syndromes (benign paroxysmal positioning vertigo—BPPV; vestibular neuritis; Menière's disease; vestibular migraine), and healthy volunteers were assessed on the Symptom-Check List 90 (a standardised, self-reporting instrument that measures psychological strain) and The structural clinical interview for DSM-IV Axis I (SCID-I). Results of the initial study (Best et al., 2006) revealed no correlation between acute (vestibular neuritis) or chronic (BPPV) vestibular dysfunction and pathology on measures of psychiatric symptoms and the authors suggested that their results did not support the hypothesis that latent vestibular dysfunction or imbalance triggers anxiety disorders. Furthering these findings, in an extension of the initial study Eckhardt-Henn et al., (2008) reported a significantly higher prevalence of psychiatric comorbidity in patients with Meniere's disease and vestibular migraine, particularly in the area of depression and anxiety. In contrast, rates of psychiatric disorders and psychological symptoms in patients with BPPV and vestibular neuritis were comparable to the control group and general population. Again the authors suggested that vestibular pathology, per se, does not increase the rate of psychological symptoms.

4.2.2. *Vestibular associations with psychosis and other psychiatric symptoms*

Beyond affective symptoms (anxiety, depression), but perhaps overlapping with the previously described cognitive deficits, peripheral vestibular dysfunction has been linked to depersonalisation/derealisation symptoms, whereby individuals experience an altered perception of their self and/or their environment (Jauregui-Renaud et al., 2008a, 2008b). In a study of 60 healthy subjects and 50 patients with peripheral vestibular disease, rates of depersonalisation/derealisation were significantly higher in vestibular patients. In line with this finding, caloric vestibular stimulation has been shown to influence body schema and internal representations of body size (Lopez et al., 2012) and galvanic vestibular stimulation has been shown to influence cognitive processes relating to body representation including tactile localisation (Ferre et al., 2013). A series of case studies has also shown caloric stimulation to improve symptoms of neglect and associated anosognosia (Cappa et al., 1987; Geminiani and Bottini, 1992; Rode et al., 1992; Ronchi et al., 2013).

In relation to other psychiatric symptoms, there are a small number of case studies that have proposed a link between symptoms of psychosis and vestibular disturbance in patients with Usher syndrome, an autosomal recessive genetic disorder manifested by hearing impairment, retinitis pigmentosa and variable vestibular deficit (Jumaian and Fergusson, 2003; Rijavec and Grubic, 2009; Wu and Chiu, 2006). These case studies all identify patients with vestibular disturbance who also experience symptoms of psychosis; however, it must be noted that Usher syndrome may involve CNS pathology beyond the vestibular system. There are also a small number of preliminary studies reporting beneficial, short term effects of caloric vestibular stimulation on symptoms of mania, delusions and insight in patients with schizophrenia and schizoaffective disorder (Dodson, 2004; Levine et al., 2012).

5. Conclusions

The first section of this literature review examined the anatomical associations between vestibular system and various psychiatric disorders. Despite the lack of direct evidence for vestibular pathology in all key psychiatric disorders reviewed, we have highlighted the substantial body of literature implicating the vestibular system in each of these key psychiatric disorders. The second part of this review provided complimentary evidence showing the link between vestibular dysfunction and vestibular stimulation upon cognitive and psychiatric symptoms. In particular, the key cognitive domain linked to vestibular function is spatial memory. Several psychiatric symptoms are commonly linked to vestibular function, including depression and anxiety with some preliminary reports of mania and psychosis also being linked to vestibular function; however, findings remain inconclusive and further research is warranted. Given the lack of biological diagnostic markers for psychiatric disorders and the associated controversies and difficulties accompanying the current subjective diagnostic assessment techniques for psychiatric illnesses (DSM-TR-IV and /V (Blais and Malone, 2013; Zimmerman, 2013)), it appears reasonable to suggest that objective measurement of the neural function of the vestibular system may provide a rich source of addition information that could provide significant insights into cognitive and psychiatric symptomatology and potentially a technique that could detect vestibular functioning could contribute to a more objective diagnosis of psychiatric illnesses.

REFERENCES

Adamec, R., et al., 2012. Activation patterns of cells in selected brain stem nuclei of more and less stress responsive rats in two animal models of PTSD—predator exposure and submersion stress. Neuropharmacology 62, 725–736.

Ahmed, F., Ras, J., Seedat, S., 2012. Volumetric structural magnetic resonance imaging findings in pediatric post-traumatic stress disorder and obsessive compulsive disorder: a systematic review. Front. Psychol. 3, 568.

Akbarian, S., Grusser, O.J., Guldin, W.O., 1994. Corticofugal connections between the cerebral cortex and brainstem vestibular nuclei in the macaque monkey. J. Comp. Neurol. 339, 421–437.

Alvarenga, P.G., et al., 2012. Obsessive–compulsive symptom dimensions correlate to specific gray matter volumes in treatment-naive patients. J. Psychiatry Res. 46, 1635–1642.

Amsterdam, J.D., et al., 2012. Greater striatal dopamine transporter density may be associated with major depressive episode. J. Affect. Disord. 141, 425–431.

Andersson, G., et al., 2003. Dual-task study of cognitive and postural interference in patients with vestibular disorders. Otol. Neurotol. 24, 289–293.

Arienzo, D., et al., 2013. Abnormal brain network organization in body dysmorphic disorder. Neuropsychopharmacology.

Arnold, J.F., et al., 2012. Fronto-limbic microstructure and structural connectivity in remission from major depression. Psychiatry Res. 204, 40–48.

Atmaca, M., et al., 2008. Hippocampus and amygdalar volumes in patients with refractory obsessive–compulsive disorder. Prog. Neuropsychopharmacol. Biol. Psychiatry 32, 1283–1286.

Atmaca, M., et al., 2010. Brain morphology of patients with body dysmorphic disorder. J. Affect. Disord. 123, 258–263.

Baba, T., et al., 2011. Association of olfactory dysfunction and brain. Metabolism in Parkinson's disease. Mov. Disord. 26, 621–628.
Bach, H., Arango, V., 2012. Neuroanatomy of serotonergic abnormalities in suicide. In: The Neurobiological Basis of Suicide. Frontiers in Neuroscience, vol., Y. Dwivedi, (Eds.), Boca Raton (FL).
Bachtold, D., et al., 2001. Spatial- and verbal-memory improvement by cold-water caloric stimulation in healthy subjects. Exp. Brain Res. 136, 128–132.
Baek, J.H., et al., 2010. Evidence that spatial memory deficits following bilateral vestibular deafferentation in rats are probably permanent. Neurobiol. Learn. Mem. 94, 402–413.
Balaban, C.D., 1996. Vestibular nucleus projections to the parabrachial nucleus in rabbits: implications for vestibular influences on the autonomic nervous system. Exp. Brain Res. 108, 367–381.
Balaban, C.D., Jacob, R.G., 2001. Background and history of the interface between anxiety and vertigo. J. Anxiety Disord. 15, 27–51.
Balaban, C.D., Thayer, J.F., 2001. Neurological bases for balance-anxiety links. J. Anxiety Disord. 15, 53–79.
Balaban, C.D., 2002. Neural substrates linking balance control and anxiety. Physiol. Behav. 77, 469–475.
Balaban, C.D., et al., 2002. Responses of primate caudal parabrachial nucleus and Kolliker-fuse nucleus neurons to whole body rotation. J. Neurophysiol. 88, 3175–3193.
Balaban, C.D., 2004a. Projections from the parabrachial nucleus to the vestibular nuclei: potential substrates for autonomic and limbic influences on vestibular responses. Brain Res. 996, 126–137.
Balaban, C.D., 2004b. Projections from the parabrachial nucleus to the vestibular nuclei: potential substrates for autonomic and limbic influences on vestibular responses. Brain Res. 996, 126–137.
Balaban, C.D., Jacob, R.G., Furman, J.M., 2011. Neurologic bases for comorbidity of balance disorders, anxiety disorders and migraine: neurotherapeutic implications. Expert. Rev. Neurother. 11, 379–394.
Baldacara, L., et al., 2008. Cerebellum and psychiatric disorders. Rev. Bras. Psiquiatr. 30, 281–289.
Baldacara, L., et al., 2011a. Reduced cerebellar left hemisphere and vermal volume in adults with PTSD from a community sample. J. Psychiatry Res. 45, 1627–1633.
Baldacara, L., et al., 2011b. Is cerebellar volume related to bipolar disorder?. J. Affect. Disord. 135, 305–309.
Baumann, B., Bogerts, B., 2001. Neuroanatomical studies on bipolar disorder. Br. J. Psychiatry Suppl. 41, s142–s147.
Bellani, M., et al., 2012. White matter microstructure alterations in bipolar disorder. Funct. Neurol. 27, 29–34.
Bennett, MR,, 2011. The prefrontal-limbic network in depression: Modulation by hypothalamus, basal ganglia and midbrain. Prog Neurobiol 93 (468), 468–487.
Bertocci, M.A., et al., 2012. Abnormal anterior cingulate cortical activity during emotional n-back task performance distinguishes bipolar from unipolar depressed females. Psychol. Med. 42, 1417–1428.
Besnard, S., et al., 2012. Influence of vestibular input on spatial and nonspatial memory and on hippocampal NMDA receptors. Hippocampus 22, 814–826.
Best, C., et al., 2006. Interaction of somatoform and vestibular disorders. J. Neurol. Neurosurg. Psychiatry 77, 658–664.
Beyer, M.K., et al., 2013. Verbal memory is associated with structural hippocampal changes in newly diagnosed Parkinson's disease. J. Neurol. Neurosurg. Psychiatry 84, 23–28.
Bing, X., et al., 2013. Alterations in the cortical thickness and the amplitude of low-frequency fluctuation in patients with post-traumatic stress disorder. Brain Res. 1490, 225–232.
Bitter, S.M., et al., 2011. Progression of amygdala volumetric abnormalities in adolescents after their first manic episode. J. Am. Acad. Child Adolesc. Psychiatry 50, 1017–1026.
Blais, M.A., Malone, J.C., 2013. Structure of the DSM-IV personality disorders as revealed in clinician ratings. Compr. Psychiatry 54, 326–333.
Bohnen, N.I., et al., 2008. Selective hyposmia in Parkinson disease: association with hippocampal dopamine activity. Neurosci. Lett. 447, 12–16.
Boos, H.B., et al., 2013. Tract-based diffusion tensor imaging in patients with schizophrenia and their non-psychotic siblings. Eur. Neuropsychopharmacol. 23, 295–304.
Bostan, A.C., Strick, P.L., 2010. The cerebellum and basal ganglia are interconnected. Neuropsychol. Rev. 20, 261–270.
Bottini, G., et al., 1994. Identification of the central vestibular projections in man: a positron emission tomography activation study. Exp. Brain Res. 99, 164–169.
Bottini, G., et al., 1995. Modulation of conscious experience by peripheral sensory stimuli. Nature 376, 778–781.
Bottini, G., et al., 2001. Cerebral representations for egocentric space: functional–anatomical evidence from caloric vestibular stimulation and neck vibration. Brain 124, 1182–1196.
Bracha, H.S., et al., 2005. Postmortem locus coeruleus neuron count in three American veterans with probable or possible war-related PTSD. J. Neuropsychiatry Clin. Neurosci. 17, 503–509.
Brandt, T., et al., 2005. Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. Brain 128, 2732–2741.
Brooks, D.J., 2010. Imaging approaches to Parkinson disease. J. Nucl. Med. 51, 596–609.
Brown, G.G., et al., 2011. Voxel-based morphometry of patients with schizophrenia or bipolar I disorder: a matched control study. Psychiatry Res. 194, 149–156.
Bruno, S., Cercignani, M., Ron, M.A., 2008. White matter abnormalities in bipolar disorder: a voxel-based diffusion tensor imaging study. Bipolar Disord. 10, 460–468.
Buchanan, B.G., et al., 2013. Brain connectivity in body dysmorphic disorder compared with controls: a diffusion tensor imaging study. Psychol. Med., 1–9.
Bush, G., Luu, P., Posner, M.I., 2000. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn. Sci. 4, 215–222.
Caixeta, G.C., Dona, F., Gazzola, J.M., 2012. Cognitive processing and body balance in elderly subjects with vestibular dysfunction. Braz. J. Otorhinolaryngol. 78, 87–95.
Cappa, S., et al., 1987. Remission of hemineglect and anosognosia during vestibular stimulation. Neuropsychologia 25, 775–782.
Carmona, J.E., Holland, A.K., Harrison, D.W., 2009. Extending the functional cerebral systems theory of emotion to the vestibular modality: a systematic and integrative approach. Psychol. Bull. 135, 286–302.
Caseras, X., et al., 2013. Ventral striatum activity in response to reward: differences between bipolar I and II disorders. Am. J. Psychiatry.
Chandley, M.J., et al., 2012. Gene expression deficits in pontine locus coeruleus astrocytes in men with major depressive disorder. J. Psychiatry Neurosci. 38, 120110.
Chao, L.L., Lenoci, M., Neylan, T.C., 2012. Effects of post-traumatic stress disorder on occipital lobe function and structure. NeuroReport 23, 412–419.
Chemerinski, E., et al., 2013. Larger putamen size in antipsychotic-naive individuals with schizotypal personality disorder. Schizophr. Res. 143, 158–164.
Chen, C.H., et al., 2011. A quantitative meta-analysis of fMRI studies in bipolar disorder. Bipolar Disord. 13, 1–15.
Chen, L., et al., 2013. White matter microstructural abnormalities in patients with late-onset schizophrenia identified by a

voxel-based diffusion tensor imaging. Psychiatry Res. 212, 201–207.
Chen, Z., et al., 2012. Voxel based morphometric and diffusion tensor imaging analysis in male bipolar patients with first-episode mania. Prog. Neuropsychopharmacol. Biol. Psychiatry 36, 231–238.
Cherkasova, M.V., Hechtman, L., 2009. Neuroimaging in attention-deficit hyperactivity disorder: beyond the frontostriatal circuitry. Can. J. Psychiatry. Rev. Canad. de Psychiatr. 54, 651–664.
Cohen, H.S., 2000. Vestibular disorders and impaired path integration along a linear trajectory. J. Vestib. Res. 10, 7–15.
Cohen, H.S., Kimball, K.T., 2008. Usefulness of some current balance tests for identifying individuals with disequilibrium due to vestibular impairments. J. Vestib. Res. 18, 295–303.
Coupland, N.J., Bell, C.J., Potokar, J.P., 1996. Serotonin reuptake inhibitor withdrawal. J. Clin. Psychopharmacol. 16, 356–362.
Cransac, H., et al., 1996. Monoamines (norepinephrine, dopamine, serotonin) in the rat medial vestibular nucleus: endogenous levels and turnover. J. Neural Transm. 103, 391–401.
Cuccurazzu, B., Halberstadt, A.L., 2008. Projections from the vestibular nuclei and nucleus prepositus hypoglossi to dorsal raphe nucleus in rats. Neurosci. Lett. 439, 70–74.
Cui, L., et al., 2011. Assessment of white matter abnormalities in paranoid schizophrenia and bipolar mania patients. Psychiatry Res. 194, 347–353.
Del Tredici, K., Braak, H., 2012. Dysfunction of the locus coeruleus-norepinephrine system and related circuitry in Parkinson's disease-related dementia. J. Neurol. Neurosurg. Psychiatry.
Delvecchio, G., et al., 2012. Common and distinct neural correlates of emotional processing in bipolar disorder and major depressive disorder: a voxel-based meta-analysis of functional magnetic resonance imaging studies. Eur. Neuropsychopharmacol. 22, 100–113.
Dickson, D.W., et al., 2010. Evidence in favor of Braak staging of Parkinson's disease. Mov. Disord. 25 (Suppl. 1), S78–S82.
Diener, C., et al., 2012. A meta-analysis of neurofunctional imaging studies of emotion and cognition in major depression. NeuroImage 61, 677–685.
Dieterich, M., Brandt, T., 2008. Functional brain imaging of peripheral and central vestibular disorders. Brain 131, 2538–2552.
Dilda, V., et al., 2012. Effects of Galvanic vestibular stimulation on cognitive function. Exp. Brain Res. 216, 275–285.
Ding, A.Y., et al., 2013. MR diffusion tensor imaging detects rapid microstructural changes in amygdala and hippocampus following fear conditioning in mice. PLoS One 8, e51704.
Dodson, M.J., 2004. Vestibular stimulation in mania: a case report. J. Neurol. Neurosurg. Psychiatry 75, 168–169.
Doty, R.L., 2012. Olfactory dysfunction in Parkinson disease. Nat. Rev. Neurol. 8, 329–339.
Dougherty, M.K., et al., 2012. Differences in subcortical structures in young adolescents at familial risk for schizophrenia: a preliminary study. Psychiatry Res. 204, 68–74.
Eagger, S., et al., 1992. Psychiatric morbidity in patients with peripheral vestibular disorder: a clinical and neuro-otological study. J. Neurol. Neurosurg. Psychiatry 55, 383–387.
Eckhardt-Henn, A., et al., 2008. Psychiatric comorbidity in different organic vertigo syndromes. J. Neurol. 255, 420–428.
Emri, M., et al., 2003. Cortical projection of peripheral vestibular signaling. J. Neurophysiol. 89, 2639–2646.
Engdahl, B., et al., 2010. Post-traumatic stress disorder: a right temporal lobe syndrome?. J. Neural. Eng. 7, 066005.
Epstein, R., Kanwisher, N., 1998. A cortical representation of the local visual environment. Nature 392, 598–601.
Etienne, A.S., Jeffery, K.J., 2004. Path integration in mammals. Hippocampus 14, 180–192.
Fan, Q., et al., 2013. Surface anatomical profile of the cerebral cortex in obsessive–compulsive disorder: a study of cortical thickness, folding and surface area. Psychol. Med. 43, 1081–1091.
Ferre, E.R., Vagnoni, E., Haggard, P., 2013. Vestibular contributions to bodily awareness. Neuropsychologia.
Feusner, J.D., Yaryura-Tobias, J., Saxena, S., 2008. The pathophysiology of body dysmorphic disorder. Body Image 5, 3–12.
Feusner, J.D., et al., 2009. Regional brain volumes and symptom severity in body dysmorphic disorder. Psychiatry Res. 172, 161–167.
Feusner, J.D., et al., 2010. Abnormalities of visual processing and frontostriatal systems in body dysmorphic disorder. Arch. Gen. Psychiatry 67, 197–205.
Feusner, J.D., et al., 2011. Abnormalities of object visual processing in body dysmorphic disorder. Psychol. Med. 41, 2385–2397.
Feusner, J.D., et al., 2013. White matter microstructure in body dysmorphic disorder and its clinical correlates. Psychiatry Res. 211, 132–140.
Filipovic, B.R., et al., 2011. Volume changes of corpus striatum, thalamus, hippocampus and lateral ventricles in post-traumatic stress disorder (PTSD) patients suffering from headaches and without therapy. Cent. Eur. Neurosurg. 72, 133–137.
Fitzgerald, P.B., et al., 2006. An analysis of functional neuroimaging studies of dorsolateral prefrontal cortical activity in depression. Psychiatry Res. 148, 33–45.
Foland-Ross, L.C., et al., 2012a. Normal amygdala activation but deficient ventrolateral prefrontal activation in adults with bipolar disorder during euthymia. NeuroImage 59, 738–744.
Foland-Ross, L.C., et al., 2012b. Mood-state effects on amygdala volume in bipolar disorder. J. Affect. Disord. 139, 298–301.
Freitag, M.T., et al., 2013. Reduced lateralization in early onset schizophrenia. Neurosci. Lett. 537, 23–28.
Frodl, T., Skokauskas, N., 2012. Meta-analysis of structural MRI studies in children and adults with attention deficit hyperactivity disorder indicates treatment effects. Acta Psychiatr. Scand. 125, 114–126.
Gazzola, J.M., et al., 2009. Factors relating to depressive symptoms among elderly people with chronic vestibular dysfunction. Arq. Neuropsiquiatr. 67, 416–422.
Geminiani, G., Bottini, G., 1992. Mental representation and temporary recovery from unilateral neglect after vestibular stimulation. J. Neurol. Neurosurg. Psychiatry 55, 332–333.
George, M.S., et al., 2008. A pilot study of vagus nerve stimulation (VNS) for treatment-resistant anxiety disorders. Brain Stimul. 1, 112–121.
Geurts, H.M., Ridderinkhof, K.R., Scholte, H.S., 2012. The relationship between grey-matter and ASD and ADHD traits in typical adults. J. Autism Dev. Disord..
Godemann, F., et al., 2004. A prospective study on the course of anxiety after vestibular neuronitis. J. Psychosom. Res. 56, 351–354.
Gonzalez, J.J., et al., 2013. Performance analysis of univariate and multivariate EEG measurements in the diagnosis of ADHD. Clin. Neurophysiol..
Gorman, J.M., et al., 2000. Neuroanatomical hypothesis of panic disorder, revised. Am. J. Psychiatry 157, 493–505.
Grabherr, L., et al., 2011. Mental transformation abilities in patients with unilateral and bilateral vestibular loss. Experimental Brain Res. Experimentelle Hirnforschung. Experimentation Cerebrale. 209, 205–214.
Graeff, F.G., 1997. Serotonergic systems. Psychiatr. Clin. North Am. 20, 723–739.
Grimm, R.J., et al., 1989. The perilymph fistula syndrome defined in mild head trauma. Acta Otolaryngol Suppl. 464, 1–40.
Guidetti, G., et al., 2008. Impaired navigation skills in patients with psychological distress and chronic peripheral vestibular

hypofunction without vertigo. Acta Otorhinolaryngol. Ital. 28, 21–25.
Hajek, T., et al., 2012. Hippocampal volumes in bipolar disorders: opposing effects of illness burden and lithium treatment. Bipolar Disord. 14, 261–270.
Halberstadt, A.L., Balaban, C.D., 2003. Organization of projections from the raphe nuclei to the vestibular nuclei in rats. Neuroscience 120, 573–594.
Halberstadt, A.L., Balaban, C.D., 2006. Serotonergic and nonserotonergic neurons in the dorsal raphe nucleus send collateralized projections to both the vestibular nuclei and the central amygdaloid nucleus. Neuroscience 140, 1067–1077.
Hale, T.S., et al., 2010. Atypical EEG beta asymmetry in adults with ADHD. Neuropsychologia 48, 3532–3539.
Halliday, G.M., 2009. Thalamic changes in Parkinson's disease. Parkinsonism Relat. Disord. 15 (Suppl. 3), S152–S155.
Harrison, B.J., et al., 2009. Altered corticostriatal functional connectivity in obsessive–compulsive disorder. Arch. Gen. Psychiatry 66, 1189–1200.
Harsanyi, A., et al., 2007. New approach to obsessive–compulsive disorder: dopaminergic theories. Psychiatr. Hung 22, 248–258.
Hart, H., et al., 2013. Meta-analysis of functional magnetic resonance imaging studies of inhibition and attention in attention-deficit/hyperactivity disorder: exploring task-specific, stimulant medication, and age effects. JAMA Psychiatry 70, 185–198.
Hashemi, E., et al., 2007. Gabrb3 gene deficient mice exhibit increased risk assessment behavior, hypotonia and expansion of the plexus of locus coeruleus dendrites. Brain Res. 1129, 191–199.
Hayashi, R., et al., 2009. Room tilt illusion in Parkinson's disease: loss of spatial reference frames?. J. Neurol. Sci. 287, 264–266.
Hayes, J.P., Hayes, S.M., Mikedis, A.M., 2012. Quantitative meta-analysis of neural activity in post-traumatic stress disorder. Biol. Mood Anxiety Disord. 2, 9.
Hegerl, U., Hensch, T., 2012. The vigilance regulation model of affective disorders and ADHD. Neurosci. Biobehav. Rev..
Herringa, R., et al., 2012. Post-traumatic stress symptoms correlate with smaller subgenual cingulate, caudate, and insula volumes in unmedicated combat veterans. Psychiatry Res. 203, 139–145.
Holroyd, C.B., N.S., Mars, R.B., Coles, M.G.H., 2004. Anterior cingulate cortex, selection for action, and error processing. In: Posner, M.I. (Ed.), Cognitive Neuroscience of Attention, vol.. Guilford Press, New York, pp. 219–231.
Hong, S.M., et al., 2013. Influence of vestibular disease on psychological distress: a multicenter study. Otolaryngol. Head Neck Surg.
Hou, J., et al., 2012. Localization of cerebral functional deficits in patients with obsessive–compulsive disorder: a resting-state fMRI study. J. Affect. Disord. 138, 313–321.
Hufner, K., et al., 2007. Spatial memory and hippocampal volume in humans with unilateral vestibular deafferentation. Hippocampus 17, 471–485.
Hummer, T.A., et al., 2013. Emotional response inhibition in bipolar disorder: a functional magnetic resonance imaging study of trait- and state-related abnormalities. Biol. Psychiatry 73, 136–143.
Ibarretxe-Bilbao, N., et al., 2011. Brain structural MRI correlates of cognitive dysfunctions in Parkinson's disease. J. Neurol. Sci. 310, 70–74.
JA., R.., 2004. Physiology of the vestibular system. In: Ototoxicity. vol., R.J. Roland PS, B.C. Decker, (Eds.), London, pp. 20–27.
James, A., et al., 2011. Structural brain and neuropsychometric changes associated with pediatric bipolar disorder with psychosis. Bipolar Disord. 13, 16–27.
Jauregui-Renaud, K., et al., 2008a. Symptoms of detachment from the self or from the environment in patients with an acquired deficiency of the special senses. J. Vestib. Res. 18, 129–137.
Jauregui-Renaud, K., et al., 2008b. Depersonalisation/derealisation symptoms and updating orientation in patients with vestibular disease. J. Neurol. Neurosurg. Psychiatry 79, 276–283.
Johnson, G.D., 1998. Medical management of migraine-related dizziness and vertigo. Laryngoscope 108, 1–28.
Jokinen, P., et al., 2013. Cognitive slowing in Parkinson's disease is related to frontostriatal dopaminergic dysfunction. J. Neurol. Sci..
Jones, M.D., Hess, E.J., 2003. Norepinephrine regulates locomotor hyperactivity in the mouse mutant coloboma. Pharmacol. Biochem. Behav. 75, 209–216.
Jones, S.M., et al., 2009. Anatomical and physiological considerations in vestibular dysfunction and compensation. Semin. Hear. 30, 231–241.
Jucaite, A., et al., 2005. Reduced midbrain dopamine transporter binding in male adolescents with attention-deficit/hyperactivity disorder: association between striatal dopamine markers and motor hyperactivity. Biol. Psychiatry 57, 229–238.
Jumaian, A., Fergusson, K., 2003. Psychosis in a patient with Usher syndrome: a case report. East. Mediterr. Health J. 9, 215–218.
Kalen, P., Karlson, M., Wiklund, L., 1985. Possible excitatory amino acid afferents to nucleus raphe dorsalis of the rat investigated with retrograde wheat germ agglutinin and D-[3H]aspartate tracing. Brain Res. 360, 285–297.
Karbasforoushan, H., Woodward, N.D., 2012. Resting-state networks in schizophrenia. Curr. Top. Med. Chem. 12, 2404–2414.
Karson, C.N., et al., 1991. The brain stem reticular formation in schizophrenia. Psychiatry Res. 40, 31–48.
Kasai, K., et al., 2003. Differences and similarities in insular and temporal pole MRI gray matter volume abnormalities in first-episode schizophrenia and affective psychosis. Arch. Gen. Psychiatry 60, 1069–1077.
Kim, B.N., et al., 2010. Regional differences in cerebral perfusion associated with the alpha-2A-adrenergic receptor genotypes in attention deficit hyperactivity disorder. J. Psychiatry Neurosci. 35, 330–336.
Kisely, M., et al., 2000. Investigation of the cerebral projection of the vestibular system using positron emission tomography. Orv. Hetil. 141, 2807–2813.
Kisely, M., et al., 2002. Changes in brain activation caused by caloric stimulation in the case of cochleovestibular denervation—PET study. Nucl. Med. Commun. 23, 967–973.
Konrad, K., et al., 2006. Dysfunctional attentional networks in children with attention deficit/hyperactivity disorder: evidence from an event-related functional magnetic resonance imaging study. Biol. Psychiatry 59, 643–651.
Koprivova, J., et al., 2009. Medial frontal and dorsal cortical morphometric abnormalities are related to obsessive–compulsive disorder. Neurosci. Lett. 464, 62–66.
Kostic, V.S., et al., 2012. Pattern of brain tissue loss associated with freezing of gait in Parkinson disease. Neurology 78, 409–416.
Kozlovsky, N., et al., 2012. Microinfusion of a corticotrophin-releasing hormone receptor 1 antisense oligodeoxynucleotide into the dorsal hippocampus attenuates stress responses at specific times after stress exposure. J. Neuroendocrinol. 24, 489–503.
Kraguljac, N.V., et al., 2012. Neurometabolites in schizophrenia and bipolar disorder—a systematic review and meta-analysis. Psychiatry Res. 203, 111–125.
Kroes, M.C., et al., 2011. Association between flashbacks and structural brain abnormalities in post-traumatic stress disorder. Eur. Psychiatry 26, 525–531.
Krogias, C., et al., 2011. Evaluation of basal ganglia, brainstem raphe and ventricles in bipolar disorder by transcranial sonography. Psychiatry Res. 194, 190–197.

Kuhn, S., et al., 2012. Reduced thickness of anterior cingulate cortex in obsessive–compulsive disorder. Cortex.
Kuhn, S., Gallinat, J., 2013. Gray matter correlates of post-traumatic stress disorder: a quantitative meta-analysis. Biol. Psychiatry. 73, 70–74.
Kusljic, S., Van Den Buuse, M., 2012. Differential role of serotonin projections from the dorsal and median raphe nuclei in phencyclidine-induced hyperlocomotion and fos-like immunoreactivity in rats. Synapse 66, 885–892.
Kuwahata, T., et al., 2002. Effects of methylphenidate on the inhibitory postsynaptic potential in rat locus coeruleus neurons. Kurume Med. J. 49, 185–190.
Landre, L., et al., 2012. Working memory processing of traumatic material in women with post-traumatic stress disorder. J. Psychiatry Neurosci. 37, 87–94.
Lazaro, L., et al., 2009. Brain changes in children and adolescents with obsessive–compulsive disorder before and after treatment: a voxel-based morphometric MRI study. Psychiatry Res. 172, 140–146.
Lazaro, L., et al., 2011. A voxel-based morphometric MRI study of stabilized obsessive–compulsive adolescent patients. Prog. Neuropsychopharmacol. Biol. Psychiatry 35, 1863–1869.
Lee, H.Y., et al., 2011. Demonstration of decreased gray matter concentration in the midbrain encompassing the dorsal raphe nucleus and the limbic subcortical regions in major depressive disorder: an optimized voxel-based morphometry study. J. Affect. Disord. 133, 128–136.
Lee, S.H., et al., 2013a. Brain volumetry in Parkinson's disease with and without dementia: where are the differences?. Acta Radiol..
Lee, S.H., et al., 2013b. Extensive white matter abnormalities in patients with first-episode schizophrenia: a diffusion tensor imaging (DTI) study. Schizophr. Res. 143, 231–238.
Levine, J., et al., 2012. Beneficial effects of caloric vestibular stimulation on denial of illness and manic delusions in schizoaffective disorder: a case report. Brain Stimul. 5, 267–273.
Levitt, J.J., et al., 2012. Fractional anisotropy and radial diffusivity: diffusion measures of white matter abnormalities in the anterior limb of the internal capsule in schizophrenia. Schizophr. Res. 136, 55–62.
Levitt, J.J., et al., 2013. A volumetric MRI study of limbic, associative and sensorimotor striatal subregions in schizophrenia. Schizophr. Res. 145, 11–19.
Lewis, S.J., et al., 2012. Anterior cingulate integrity: executive and neuropsychiatric features in Parkinson's disease. Mov. Disord. 27, 1262–1267.
Liao, Y., et al., 2013. Is depression a disconnection syndrome? Meta-analysis of diffusion tensor imaging studies in patients with MDD. J. Psychiatry Neurosci. 38, 49–56.
Licata, F., et al., 1995. Neuronal responses in vestibular nuclei to dorsal raphe electrical activation. J. Vestib. Res. 5, 137–145.
Lim, C.S., et al., 2013. Longitudinal neuroimaging and neuropsychological changes in bipolar disorder patients: review of the evidence. Neurosci. Biobehav. Rev. 37, 418–435.
Lin, F., et al., 2011. Abnormal frontal cortex white matter connections in bipolar disorder: a DTI tractography study. J. Affect. Disord. 131, 299–306.
Linnman, C., et al., 2011. An fMRI study of unconditioned responses in post-traumatic stress disorder. Biol. Mood Anxiety Disord. 1, 8.
Liu, C.H., et al., 2012a. Abnormal baseline brain activity in bipolar depression: a resting state functional magnetic resonance imaging study. Psychiatry Res. 203, 175–179.
Liu, C.H., et al., 2012b. Regional homogeneity within the default mode network in bipolar depression: a resting-state functional magnetic resonance imaging study. PLoS One 7, e48181.
Liu, C.H., et al., 2013. Regional homogeneity of resting-state brain abnormalities in bipolar and unipolar depression. Prog. Neuropsychopharmacol. Biol. Psychiatry 41, 52–59.
Lopez-Larson, M.P., et al., 2012. Reduced insular volume in attention deficit hyperactivity disorder. Psychiatry Res. 204, 32–39.
Lopez, C., et al., 2012. Vestibular stimulation modifies the body schema. Neuropsychologia 50, 1830–1837.
Lopez, C., Blanke, O., 2011. The thalamocortical vestibular system in animals and humans. Brain Res. Rev. 67, 119–146.
Lopez, C., Blanke, O., Mast, F.W., 2012. The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. Neuroscience 212, 159–179.
Lorenzetti, V., et al., 2010. Amygdala volumes in a sample of current depressed and remitted depressed patients and healthy controls. J. Affect. Disord. 120, 112–119.
Luo, F.F., Han, F., Shi, Y.X., 2011. Changes in 5-HT1A receptor in the dorsal raphe nucleus in a rat model of post-traumatic stress disorder. Mol. Med. Rep. 4, 843–847.
Luppi, P.H., et al., 1995. Afferent projections to the rat locus coeruleus demonstrated by retrograde and anterograde tracing with cholera-toxin B subunit and Phaseolus vulgaris leucoagglutinin. Neuroscience 65, 119–160.
Ma, Q., et al., 2013. Altered cerebellar-cerebral resting-state functional connectivity reliably identifies major depressive disorder. Brain Res. 1495, 86–94.
Machado, M.L., et al., 2012. Influence of anxiety in spatial memory impairments related to the loss of vestibular function in rat. Neuroscience 218, 161–169.
Maguire, E.A., Frackowiak, R.S., Frith, C.D., 1997. Recalling routes around london: activation of the right hippocampus in taxi drivers. J. Neurosci. 17, 7103–7110.
Mahon, P.B., et al., 2012. An MRI study of amygdala in schizophrenia and psychotic bipolar disorder. Schizophr. Res. 138, 188–191.
Maier, S.J., et al., 2013. Altered cingulate and amygdala response towards threat and safe cues in attention deficit hyperactivity disorder. Psychol. Med., 1–14.
Maller, J.J., Daskalakis, Z.J., Fitzgerald, P.B., 2007. Hippocampal volumetrics in depression: the importance of the posterior tail. Hippocampus 17, 1023–1027.
Maller, J.J., et al., 2012a. Hippocampal volumetrics in treatment-resistant depression and schizophrenia: the devil's in de-tail. Hippocampus 22, 9–16.
Maller, J.J., et al., 2012b. The (eigen) value of diffusion tensor imaging to investigate depression after traumatic brain injury. Hum. Brain Mapp..
Malykhin, N.V., et al., 2012. Fronto-limbic volumetric changes in major depressive disorder. J. Affect. Disord. 136, 1104–1113.
Mamoto, Y., et al., 2002. Three-dimensional analysis of human locomotion in normal subjects and patients with vestibular deficiency. Acta Otolaryngol. 122, 495–500.
Manzoni, D., et al., 1989. Responses of locus coeruleus neurons to convergent neck and vestibular inputs. Acta Otolaryngol Suppl. 468, 129–135.
Marchand, W.R., et al., 2012. Aberrant functional connectivity of cortico-basal ganglia circuits in major depression. Neurosci. Lett. 514, 86–90.
Marner, L., Soborg, C., Pakkenberg, B., 2005. Increased volume of the pigmented neurons in the locus coeruleus of schizophrenic subjects: a stereological study. J. Psychiatry Res. 39, 337–345.
Marsh, R., et al., 2013. Altered activation in fronto-striatal circuits during sequential processing of conflict in unmedicated adults with obsessive–compulsive disorder. Biol. Psychiatry.
Massat, I., et al., 2012. Working memory-related functional brain patterns in never medicated children with ADHD. PLoS One 7, e49392.

Matthews, P.R., Harrison, P.J., 2012. A morphometric, immunohistochemical, and in situ hybridization study of the dorsal raphe nucleus in major depression, bipolar disorder, schizophrenia, and suicide. J. Affect. Disord. 137, 125–134.
Mazaheri, A., et al., 2010. Functional disconnection of frontal cortex and visual cortex in attention-deficit/hyperactivity disorder. Biol. Psychiatry 67, 617–623.
Mehnert, S., et al., 2010. Transcranial sonography for diagnosis of Parkinson's disease. BMC Neurol. 10, 9.
Metzger, L.J., et al., 2004. PTSD arousal and depression symptoms associated with increased right-sided parietal EEG asymmetry. J. Abnorm. Psychol. 113, 324–329.
Mickleborough, M.J., et al., 2011. Effects of trauma-related cues on pain processing in post-traumatic stress disorder: an fMRI investigation. J. Psychiatry Neurosci. 36, 6–14.
Mills, K.L., et al., 2012. Altered cortico-striatal-thalamic connectivity in relation to spatial working memory capacity in children with ADHD. Front. Psychiatry 3, 2.
Moresco, R.M., et al., 2007. Fluvoxamine treatment and D2 receptors: a pet study on OCD drug-naive patients. Neuropsychopharmacology 32, 197–205.
Morey, R.A., et al., 2012. Amygdala volume changes in post-traumatic stress disorder in a large case-controlled veterans group. Arch. Gen. Psychiatry 69, 1169–1178.
Nagel, B.J., et al., 2011. Altered white matter microstructure in children with attention-deficit/hyperactivity disorder. J. Am. Acad. Child Adolesc. Psychiatry 50, 283–292.
Nakamae, T., et al., 2012. Reduced cortical thickness in non-medicated patients with obsessive–compulsive disorder. Prog. Neuropsychopharmacol. Biol. Psychiatry 37, 90–95.
Nardo, D., Santangelo, V., Macaluso, E., 2011. Stimulus-driven orienting of visuo-spatial attention in complex dynamic environments. Neuron 69, 1015–1028.
Nazari, M.A., et al., 2010. Visual sensory processing deficit in the occipital region in children with attention-deficit/hyperactivity disorder as revealed by event-related potentials during cued continuous performance test. Neurophysiol. Clin. 40, 137–149.
Nicoletti, G., et al., 2006. MR imaging of middle cerebellar peduncle width: differentiation of multiple system atrophy from Parkinson disease. Radiology 239, 825–830.
Nikolaus, S., et al., 2010. Cortical GABA, striatal dopamine and midbrain serotonin as the key players in compulsive and anxiety disorders—results from in vivo imaging studies. Rev. Neurosci. 21, 119–139.
Nishida, S., et al., 2011. Anterior insular volume is larger in patients with obsessive–compulsive disorder. Prog. Neuropsychopharmacol. Biol. Psychiatry 35, 997–1001.
O'Donnell, T., Hegadoren, K.M., Coupland, N.C., 2004. Noradrenergic mechanisms in the pathophysiology of post-traumatic stress disorder. Neuropsychobiology 50, 273–283.
Ohtsuka, C., et al., 2013. Changes in substantia nigra and locus coeruleus in patients with early-stage Parkinson's disease using neuromelanin-sensitive MR imaging. Neurosci. Lett..
Ordway, G.A., et al., 2012. Low gene expression of bone morphogenetic protein 7 in brainstem astrocytes in major depression. Int. J. Neuropsychopharmacol. 15, 855–868.
Orosz, A., et al., 2012. Reduced cerebral blood flow within the default-mode network and within total gray matter in major depression. Brain Connect. 2, 303–310.
Ossenkopp, K.P., Hargreaves, E.L., 1993. Spatial learning in an enclosed eight-arm radial maze in rats with sodium arsanilate-induced labyrinthectomies. Behav. Neural Biol. 59, 253–257.
Palaniyappan, L., Liddle, P.F., 2012. Dissociable morphometric differences of the inferior parietal lobule in schizophrenia. Eur. Arch. Psychiatry Clin. Neurosci. 262, 579–587.
Palma, M., et al., 2012. An OCD patient presenting with a cerebellum venous variant in a family with a strong schizophrenia loading: a case report. Innov. Clin. Neurosci. 9, 18–20.
Parnaudeau, S., et al., 2013. Inhibition of mediodorsal thalamus disrupts thalamofrontal connectivity and cognition. Neuron 77, 1151–1162.
Pelled, G., et al., 2007. Manganese-enhanced MRI in a rat model of Parkinson's disease. J. Magn. Reson. Imaging 26, 863–870.
Peng, D.H., et al., 2011. Decreased regional homogeneity in major depression as revealed by resting-state functional magnetic resonance imaging. Chin. Med. J. (Engl.) 124, 369–373.
Peng, H.J., et al., 2013. Abnormalities of cortical-limbic-cerebellar white matter networks may contribute to treatment-resistant depression: a diffusion tensor imaging study. BMC Psychiatry 13, 72.
Peruch, P., et al., 1999. Spatial performance of unilateral vestibular defective patients in nonvisual versus visual navigation. J. Vestib. Res. 9, 37–47.
Petrosini, L., Dell'Anna, M.E., 1993. Vestibular compensation is affected by treatment with dopamine active agents. Arch. Ital. Biol. 131, 159–171.
Pittenger, C., Bloch, M., Wegner, R., Teitelbaum, C., Krystal, J.H., Coric, V., 2006. Glutamatergic dysfunction in obsessive–compulsive disorder and the potential clinical utility of glutamate-modulating agents. Prim. Psychiatry, 65–77.
Planetta, P.J., et al., 2013. Thalamic projection fiber integrity in de novo Parkinson disease. AJNR Am. J. Neuroradiol. 34, 74–79.
Poissant, H., Mendrek, A., Senhadji, N., 2012. Neural correlates of forethought in ADHD. J. Atten. Disord..
Pollak, L., et al., 2003. Anxiety in the first attack of vertigo. Otolaryngol. Head Neck Surg. 128, 829–834.
Premkumar, P., et al., 2010. N-acetyl aspartate concentration in the anterior cingulate cortex in patients with schizophrenia: a study of clinical and neuropsychological correlates and preliminary exploration of cognitive behaviour therapy effects. Psychiatry Res. 182, 251–260.
Qin, L.D., et al., 2012. A preliminary study of alterations in default network connectivity in post-traumatic stress disorder patients following recent trauma. Brain Res. 1484, 50–56.
Rabinak, C.A., et al., 2011. Altered amygdala resting-state functional connectivity in post-traumatic stress disorder. Front. Psychiatry 2, 62.
Radua, J., Mataix-Cols, D., 2009. Voxel-wise meta-analysis of grey matter changes in obsessive–compulsive disorder. Br. J. Psychiatry 195, 393–402.
Rae, C.L., et al., 2012. White matter pathology in Parkinson's disease: the effect of imaging protocol differences and relevance to executive function. NeuroImage 62, 1675–1684.
Ramos-Quiroga, J.A., et al., 2013. The neuroanatomy of attention deficit hyperactivity disorder in adults: structural and functional neuroimaging findings. Rev. Neurol. 56 (Suppl. 1), S93–S106.
Redfern, M.S., et al., 2004. Cognitive influences in postural control of patients with unilateral vestibular loss. Gait Posture 19, 105–114.
Rigucci, S., et al., 2012. Anatomical substrates of cognitive and clinical dimensions in first episode schizophrenia. Acta Psychiatr. Scand..
Rijavec, N., Grubic, V.N., 2009. Usher syndrome and psychiatric symptoms: a challenge in psychiatric management. Psychiatr. Danub. 21, 68–71.
Risey, J., Briner, W., 1990. Dyscalculia in patients with vertigo. J. Vestib. Res. 1, 31–37.
Rochefort, C., Lefort, J., Rondi-Reig, L., 2013. The cerebellum: a new key structure in the navigation system. Front. Neural. Circuits 7, 35.
Rode, G., et al., 1992. Partial remission of hemiplegia and somatoparaphrenia through vestibular stimulation in a case of unilateral neglect. Cortex 28, 203–208.

Ronchi, R., et al., 2013. Remission of anosognosia for right hemiplegia and neglect after caloric vestibular stimulation. Restor. Neurol. Neurosci. 31, 19–24.
Rossi, R., et al., 2012. Volumetric and topographic differences in hippocampal subdivisions in borderline personality and bipolar disorders. Psychiatry Res. 203, 132–138.
Sacher, J., et al., 2012. Mapping the depressed brain: a meta-analysis of structural and functional alterations in major depressive disorder. J. Affect. Disord. 140, 142–148.
Salerian, A.J., Altar, C.A., 2012. The prefrontal cortex influence over subcortical and limbic regions governs antidepressant response by N=H/(M+R). Psychiatry Res. 204, 1–12.
Sanderson, T.M., et al., 2012. Alterations in hippocampal excitability, synaptic transmission and synaptic plasticity in a neurodevelopmental model of schizophrenia. Neuropharmacology 62, 1349–1358.
Sara, S.J., 2009. The locus coeruleus and noradrenergic modulation of cognition. Nat. Rev. Neurosci. 10, 211–223.
Sartory, G., et al., 2013. In search of the trauma memory: a meta-analysis of functional neuroimaging studies of symptom provocation in post-traumatic stress disorder (PTSD). PLoS One 8, e58150.
Sasaki, M., et al., 2008. Monoamine neurons in the human brain stem: anatomy, magnetic resonance imaging findings, and clinical implications. NeuroReport 19, 1649–1654.
Schautzer, F., et al., 2003. Spatial memory deficits in patients with chronic bilateral vestibular failure. Ann. N. Y. Acad. Sci. 1004, 316–324.
Schneider, M.F., et al., 2010. Impairment of fronto-striatal and parietal cerebral networks correlates with attention deficit hyperactivity disorder (ADHD) psychopathology in adults—a functional magnetic resonance imaging (fMRI) study. Psychiatry Res. 183, 75–84.
Schrader, L.M., et al., 2011. Trigeminal nerve stimulation in major depressive disorder: first proof of concept in an open pilot trial. Epilepsy Behav. 22, 475–478.
Schubert, M.C., Minor, L.B., 2004. Vestibulo-ocular physiology underlying vestibular hypofunction. Phys. Ther. 84, 373–385.
Schuerger, R.J., Balaban, C.D., 1999. Organization of the coeruleo-vestibular pathway in rats, rabbits, and monkeys. Brain Res. Brain Res. Rev. 30, 189–217.
Seager, M.A., et al., 2005. Chronic coadministration of olanzapine and fluoxetine activates locus coeruleus neurons in rats: implications for bipolar disorder. Psychopharmacology (Berl.) 181, 126–133.
Segura, B., et al., 2013. Progressive changes in a recognition memory network in Parkinson's disease. J. Neurol. Neurosurg. Psychiatry 84, 370–378.
Seidman, L.J., et al., 2011. Gray matter alterations in adults with attention-deficit/hyperactivity disorder identified by voxel based morphometry. Biol. Psychiatry 69, 857–866.
Sexton, C.E., Mackay, C.E., Ebmeier, K.P., 2013. A systematic review and meta-analysis of magnetic resonance imaging studies in late-life depression. Am. J. Geriatr. Psychiatry 21, 184–195.
Sharp, P.E., et al., 1995. Influences of vestibular and visual motion information on the spatial firing patterns of hippocampal place cells. J. Neurosci. 15, 173–189.
Shibata, E., et al., 2008. Use of neuromelanin-sensitive MRI to distinguish schizophrenic and depressive patients and healthy individuals based on signal alterations in the substantia nigra and locus ceruleus. Biol. Psychiatry 64, 401–406.
Shin, L.M., Rauch, S.L., Pitman, R.K., 2006. Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. Ann. N. Y. Acad. Sci. 1071, 67–79.
Shucard, J.L., et al., 2012. Symptoms of post-traumatic stress disorder and exposure to traumatic stressors are related to brain structural volumes and behavioral measures of affective stimulus processing in police officers. Psychiatry Res. 204, 25–31.
Silk, T.J., et al., 2009. White-matter abnormalities in attention deficit hyperactivity disorder: a diffusion tensor imaging study. Hum. Brain Mapp. 30, 2757–2765.
Sioka, C., Fotopoulos, A., Kyritsis, A.P., 2010. Recent advances in PET imaging for evaluation of Parkinson's disease. Eur. J. Nucl. Med. Mol. Imaging 37, 1594–1603.
Sliz, D., Hayley, S., 2012. Major depressive disorder and alterations in insular cortical activity: a review of current functional magnetic imaging research. Front. Hum. Neurosci. 6, 323.
Smith, P.F., 2012. Dyscalculia and vestibular function. Med. Hypotheses. 79, 493–496.
Smith, P.F., et al., 2010. Modulation of memory by vestibular lesions and galvanic vestibular stimulation. Front. Neurol. 1, 141.
Smith, P.F., Haslett, S., Zheng, Y., 2013. A multivariate statistical and data mining analysis of spatial memory-related behaviour following bilateral vestibular loss in the rat. Behav. Brain Res. 246C, 15–23.
Smith, P.F., Darlington, C.L., 1994. Pharmacology of the vestibular system. Baillieres Clin. Neurol. 3, 467–484.
Smith, P.F., 1997. Vestibular–hippocampal interactions. Hippocampus 7, 465–471.
Smith, P.F., et al., 2005a. The effects of vestibular lesions on hippocampal function in rats. Prog. Neurobiol. 75, 391–405.
Smith, P.F., et al., 2005b. Does vestibular damage cause cognitive dysfunction in humans?. J. Vestib. Res. 15, 1–9.
Song, A., et al., 2011a. Disproportionate alterations in the anterior and posterior insular cortices in obsessive–compulsive disorder. PLoS One 6, e22361.
Song, S.K., et al., 2011b. The pattern of cortical atrophy in patients with Parkinson's disease according to cognitive status. Mov. Disord. 26, 289–296.
Sripada, R.K., et al., 2012. Altered resting-state amygdala functional connectivity in men with post-traumatic stress disorder. J. Psychiatry Neurosci. 37, 241–249.
Stackman, R.W., Clark, A.S., Taube, J.S., 2002. Hippocampal spatial representations require vestibular input. Hippocampus 12, 291–303.
Stackman, R.W., Herbert, A.M., 2002. Rats with lesions of the vestibular system require a visual landmark for spatial navigation. Behav. Brain Res. 128, 27–40.
Stuhrmann, A., et al., 2012. Mood-congruent amygdala responses to subliminally presented facial expressions in major depression: associations with anhedonia. J. Psychiatry Neurosci. 37, 120060.
Sullivan, G.M., et al., 2013. Higher in vivo serotonin-1a binding in post-traumatic stress disorder: a pet study with [(11) C]way-100635. Depress. Anxiety 30, 197–206.
Sun, L., et al., 2012. Abnormal functional connectivity between the anterior cingulate and the default mode network in drug-naive boys with attention deficit hyperactivity disorder. Psychiatry Res. 201, 120–127.
Szeszko, P.R., et al., 1999. Orbital frontal and amygdala volume reductions in obsessive–compulsive disorder. Arch. Gen. Psychiatry 56, 913–919.
Szeszko, P.R., et al., 2005. White matter abnormalities in first-episode schizophrenia or schizoaffective disorder: a diffusion tensor imaging study. Am. J. Psychiatry 162, 602–605.
Takahashi, T., et al., 2004. Bilateral volume reduction of the insular cortex in patients with schizophrenia: a volumetric MRI study. Psychiatry Res. 131, 185–194.
Takahashi, T., et al., 2010. Volumetric MRI study of the insular cortex in individuals with current and past major depression. J. Affect. Disord. 121, 231–238.
Talkowski, M.E., et al., 2005. Cognitive requirements for vestibular and ocular motor processing in healthy adults and patients with unilateral vestibular lesions. J. Cogn. Neurosci. 17, 1432–1441.

Taube, J.S., et al., 1996. Processing the head direction cell signal: a review and commentary. Brain Res. Bull. 40, 477–484 (discussion 484-6).
Tavanti, M., et al., 2012. Evidence of diffuse damage in frontal and occipital cortex in the brain of patients with post-traumatic stress disorder. Neurol. Sci. 33, 59–68.
Tessitore, A., et al., 2012a. Resting-state brain connectivity in patients with Parkinson's disease and freezing of gait. Parkinsonism Relat. Disord. 18, 781–787.
Tessitore, A., et al., 2012b. Default-mode network connectivity in cognitively unimpaired patients with Parkinson disease. Neurology 79, 2226–2232.
Thomaes, K., et al., 2010. Reduced anterior cingulate and orbitofrontal volumes in child abuse-related complex PTSD. J. Clin. Psychiatry 71, 1636–1644.
Tobe, R.H., et al., 2010. Cerebellar morphology in Tourette syndrome and obsessive–compulsive disorder. Ann. Neurol. 67, 479–487.
Townsend, J., Altshuler, L.L., 2012. Emotion processing and regulation in bipolar disorder: a review. Bipolar Disord. 14, 326–339.
Trinh, J.V., et al., 2003. Differential psychostimulant-induced activation of neural circuits in dopamine transporter knockout and wild type mice. Neuroscience 118, 297–310.
Tsujimoto, S., et al., 2013. Increased prefrontal oxygenation related to distractor-resistant working memory in children with attention-deficit/hyperactivity disorder (ADHD). Child Psychiatry Hum. Dev..
Tuohimaa, P., et al., 1983. Studies of vestibular cortical areas with short-living $15O_2$ isotopes. ORL J. Otorhinolaryngol. Relat. Spec. 45, 315–321.
van den Heuvel, O.A., et al., 2005. Disorder-specific neuroanatomical correlates of attentional bias in obsessive–compulsive disorder, panic disorder, and hypochondriasis. Arch. Gen. Psychiatry 62, 922–933.
van Ewijk, H., et al., 2012. Diffusion tensor imaging in attention deficit/hyperactivity disorder: a systematic review and meta-analysis. Neurosci. Biobehav. Rev. 36, 1093–1106.
Van Rheenen, T.E., Rossell, S.L., 2012. Genetic and neurocognitive foundations of emotion abnormalities in bipolar disorder. Cogn. Neuropsychiatry.
Velikova, S., et al., 2010. Dysfunctional brain circuitry in obsessive–compulsive disorder: source and coherence analysis of EEG rhythms. NeuroImage 49, 977–983.
Vibert, N., et al., 1995. Dopaminergic agonists have both presynaptic and postsynaptic effects on the guinea-pig's medial vestibular nucleus neurons. Eur. J. Neurosci. 7, 555–562.
Vitte, E., et al., 1996. Activation of the hippocampal formation by vestibular stimulation: a functional magnetic resonance imaging study. Exp. Brain Res. Experimentelle Hirnforschung. Experimentation Cerebrale 112, 523–526.
Wang, Y., et al., 2012. Different iron-deposition patterns of multiple system atrophy with predominant parkinsonism and idiopathetic Parkinson diseases demonstrated by phase-corrected susceptibility-weighted imaging. AJNR Am. J. Neuroradiol. 33, 266–273.
Wenzel, R., et al., 1996. Deactivation of human visual cortex during involuntary ocular oscillations. A PET activation study. Brain 119 (Pt. 1), 101–110.
Whalley, M.G., et al., 2013. An fMRI investigation of posttraumatic flashbacks. Brain Cogn. 81, 151–159.
Winter, L., et al., 2012. Vestibular stimulation on a motion-simulator impacts on mood States. Front. Psychol. 3, 499.
Wiste, A.K., et al., 2008. Norepinephrine and serotonin imbalance in the locus coeruleus in bipolar disorder. Bipolar Disord. 10, 349–359.
Wu, C.Y., Chiu, C.C., 2006. Usher syndrome with psychotic symptoms: two cases in the same family. Psychiatry Clin. Neurosci. 60, 626–628.
Xia, S., et al., 2012. Thalamic shape and connectivity abnormalities in children with attention-deficit/hyperactivity disorder. Psychiatry Res. 204, 161–167.
Yardley, L., et al., 1999. Relationship between physical and psychosocial dysfunction in Mexican patients with vertigo: a cross-cultural validation of the vertigo symptom scale. J. Psychosom. Res. 46, 63–74.
Yaryura-Tobias, J.A., Neziroglu, F., Torres-Gallegos, M., 2002. Neuroanatomical correlates and somatosensorial disturbances in body dysmorphic disorder. CNS Spectr. 7, 432–434.
Yates, B.J., Miller, A.D., 1998. Physiological evidence that the vestibular system participates in autonomic and respiratory control. J. Vestib. Res. 8, 17–25.
Yin, Y., et al., 2011. Altered resting-state functional connectivity of thalamus in earthquake-induced post-traumatic stress disorder: a functional magnetic resonance imaging study. Brain Res. 1411, 98–107.
Yucel, K., et al., 2012. Cerebellar vermis volume in major depressive disorder. Brain Struct. Funct..
Zarei, M., et al., 2011. Changes in gray matter volume and white matter microstructure in adolescents with obsessive–compulsive disorder. Biol. Psychiatry 70, 1083–1090.
Zeng, L.L., et al., 2012. Antidepressant treatment normalizes white matter volume in patients with major depression. PLoS One 7, e44248.
Zheng, Y., Darlington, C.L., Smith, P.F., 2004. Bilateral labyrinthectomy causes long-term deficit in object recognition in rat. NeuroReport 15, 1913–1916.
Zheng, Y., et al., 2009a. Bilateral vestibular deafferentation causes deficits in a 5-choice serial reaction time task in rats. Behav. Brain Res. 203, 113–117.
Zheng, Y., et al., 2009b. Long-term deficits on a foraging task after bilateral vestibular deafferentation in rats. Hippocampus 19, 480–486.
Zhu, M.Y., et al., 1999. Elevated levels of tyrosine hydroxylase in the locus coeruleus in major depression. Biol. Psychiatry 46, 1275–1286.
Zimmerman, M., 2013. Would broadening the diagnostic criteria for bipolar disorder do more harm than good? Implications from longitudinal studies of subthreshold conditions. J. Clin. Psychiatry 73, 437–443.
zu Eulenburg, P., et al., 2012. Meta-analytical definition and functional connectivity of the human vestibular cortex. NeuroImage 60, 162–169.
Zuo, C., et al., 2013. Metabolic imaging of bilateral anterior capsulotomy in refractory obsessive compulsive disorder: an FDG PET study. J. Cereb. Blood Flow Metab..
Zuo, N., et al., 2012. White matter abnormalities in major depression: a tract-based spatial statistics and rumination study. PLoS One 7, e37561.