# BRAIN MAPPING
# AN ENCYCLOPEDIC REFERENCE

Volume 2

**Anatomy and Physiology**
**Systems**

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## Volume 2

## Anatomy and Physiology
## Systems


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*University of Southern California, Los Angeles, CA, USA*

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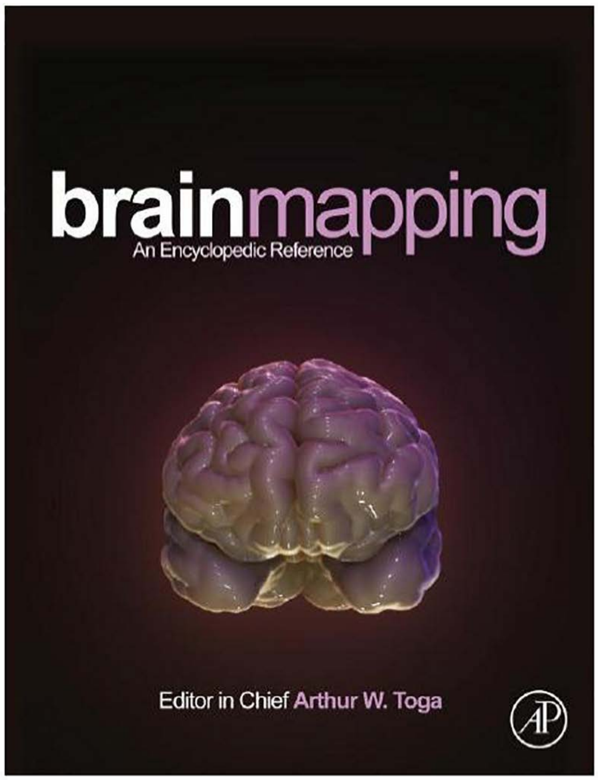


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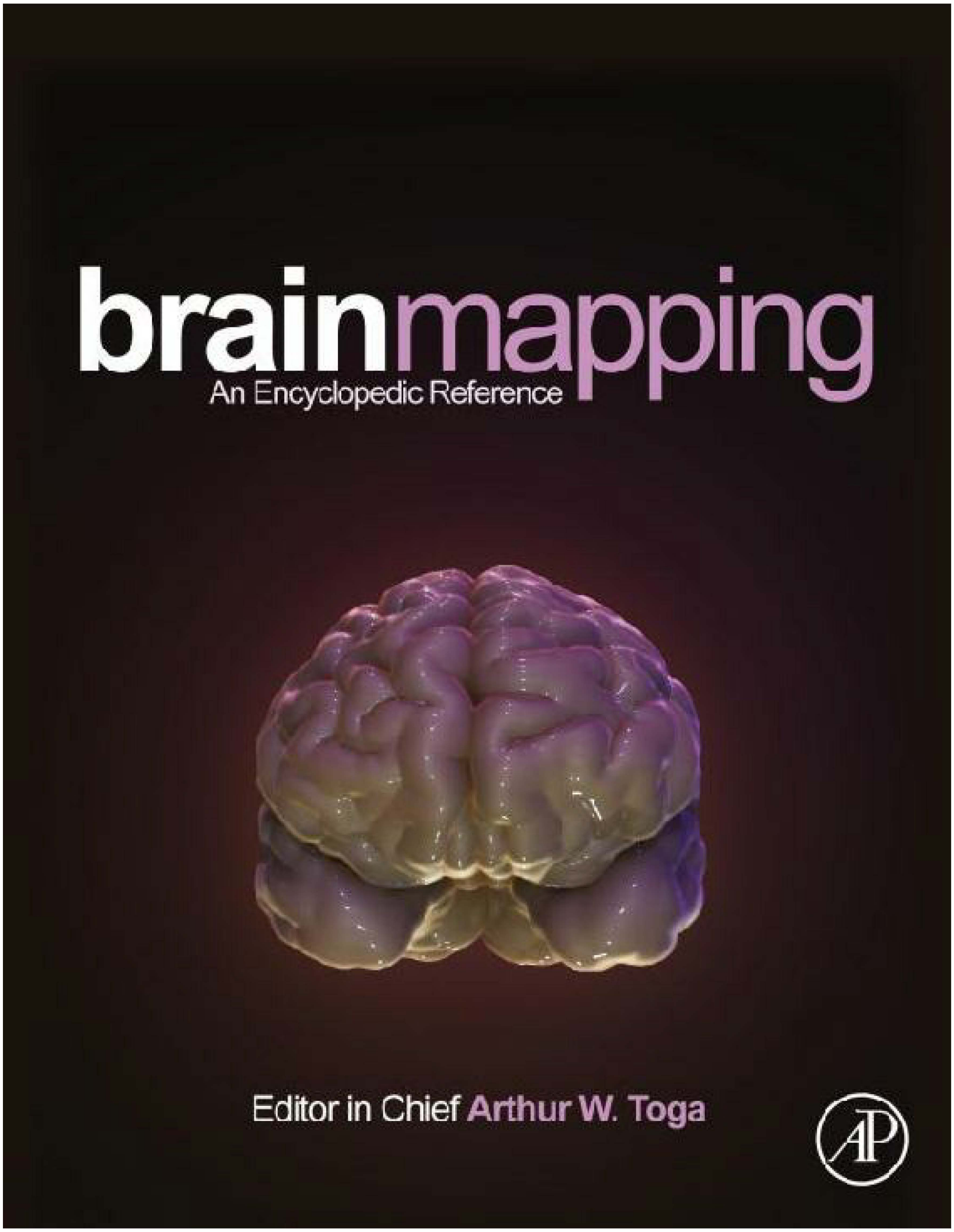

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Neural Correlates of Motor Deficits in Young Patients with Traumatic Brain Injury

K Caeyenberghs, University of Ghent, Ghent, Belgium

SP Swinnen, Group Biomedical Sciences, KU Leuven, Belgium

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Glossary

MRI technology that measures brain activity during tasks by

Diffuse axonal injury (DAI) Widespread damage to white

detecting associated changes in blood flow.

matter tracts and projections to the cortex after traumatic

Resting-state fMRI (rs-fMRI) A method of functional brain

brain injury.

imaging that can be used to evaluate regional interactions

Diffusion tensor imaging (DTI) An MRI technique that

that occur when a subject is not performing an explicit task.

enables the measurement of the restricted diffusion of water

Traumatic brain injury (intracranial injury) Injury that

in tissue in order to produce neural tract images.

occurs when an external force traumatically injures the brain

Functional magnetic resonance imaging or functional

(such as a traffic accident, fall, or sport injury).

MRI (fMRI) A functional neuroimaging procedure using

Motor Deficits in Young Patients with Traumatic

TBI regain independent ambulation, but balance and speed

Brain Injury

remain frequently impaired (Brink et al., 1970; Van der Schaaf et al., 1997). Rossi and Sullivan (1996) found deficits in

Acquired brain injury (ABI) is one of the leading causes of death

strength, agility, and coordination about 4 years after injury,

or permanent disability in children and adolescents in the

which limited the children's participation in sports and other

United States. Approximately 200 000 patients with pediatric

physical activities. Other studies reported low performance on

brain injury are hospitalized each year, and of these children,

fine motor tasks involving upper-limb speed and dexterity

30 000 suffer permanent disability (Guyer & Ellers, 1990).

more than 1 year after TBI (Asikainen et al., 1999; Chaplin

Although this figure is extremely large, it may underestimate

et al., 1993; Wallen et al., 2001). Few studies, however, have

the true burden of ABI, as many individuals with milder injuries

used instrumented quantitative measures to assess the recovery

are often unknown to the medical system (Langlois et al.,

of sensorimotor functions after TBI. Detailed quantitative ana-

2006). ABI can result from multiple causes, including trauma lyses of motor behavior can objectify performance levels that

(motor vehicle accidents, bicycle accidents, falls, and sport

are not clearly visible with the naked eye and may contribute to

injuries), central nervous system infections, noninfectious disboth evaluation of rehabilitation and a better understanding of orders (epilepsy, hypoxia/ischemia, and genetic/metabolic the relationship between brain injury and ensuing deficits. disorders), tumors, and vascular abnormalities (Atabaki, Therefore, in our previous studies (Caeyenberghs et al., 2007). Although there are many causes of ABI in children, 2009a, 2009b; 2010a, 2010b; see Table 1), impairments of traumatic brain injury (TBI) is by far the most common. The relevant functional motor tasks, that is, postural control and severity of such injuries may range from 'mild,' that is, a brief eye–hand coordination, were assessed with instrumented mea- change in mental status or consciousness, to 'severe,' that is, an sures in children with ABI. Both functions are essential for many extended period of unconsciousness or amnesia after the injury. activities of daily living. Moreover, both tasks reveal different More than 450 000 children under the age of 14 years are aspects of motor performance and rely on very different brain admitted to the emergency department each year for TBI in the structures, underscoring their complementarity.

United States (Langlois et al., 2006). Although considerable First, the interactive technology and clinically proven pro-

strides have been made in decreasing overall TBI-related mor-
tocols of the NeuroCom system allowed us to objectively and
tality by the application of evidence-based medicine, many
systematically assess balance control (Caeyenberghs et al.,
individuals develop chronic problems, often resulting in life-
2010a, 2010b). As part of the EquiTest system, the Sensory
long disability.

Organization Test (SOT) protocol systematically disrupted the
The clinical outcome in pediatric TBI is highly variable but
sensory selection processes (i.e., somatosensory, visual inputs, or
often includes persistent cognitive problems such as attention
both) while measuring a subject's ability to maintain equilib-
deficit, memory impairment, slowed processing speed, word-
rium. Six sensory conditions evaluated the relative contributions
finding difficulties, impaired executive function, behavioral
of vision, vestibular, and somatosensory inputs in balance func-
disinhibition, and emotional lability (Taylor, 2004; Yeates &
tion. In condition 1, all three sensory systems were operational
Taylor, 2005). Motor disabilities are often less obvious in
while the participant stood on a fixed platform with eyes open,

children with TBI than in children with cerebral palsy and are

and a baseline measure of stability was obtained. Condition 2

sometimes considered a less pervasive problem than cognitive

was the same as condition 1, except that the eyes were closed.

deficits (Bowen et al., 1997; Emanuelson et al., 1998). Never-Condition 3 was similar to condition 1 but the visual surround

theless, several studies reported long-lasting deficits in motor

moved to track the participant’s sway, which provided inaccurate

proficiency of children after TBI, which can lead to significant

orientation cues. In condition 4, the subject stood with the eyes

functional losses. The majority of children sustaining severe

open and the visual surround fixed but the platform moved in

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Table 1

Overview of the different studies

Mean age at

N

Description of the participants and methods

Mean age

injury

Caeyenberghs et al.

28 ABI and 28

Traumatic brain injury (N ¼ 14), surgery (N ¼ 6), vascular disease

11 years 9

9 years 4

(2009a)

controls

(N ¼ 6), infections (N ¼ 2)

months

months

Tracking tasks (feedback and feedforward)

Caeyenberghs et al.

9 TBI and 17

Traumatic brain injury (no focal lesions)

12 years

9 years 10

(2009b)

controls

Task-related fMRI (coordination task)

8 months

months

Caeyenberghs et al.

12 TBI and 14

Traumatic brain injury

14 years

10 years 6

(2010a)

controls

Instrumented motor task: SOT protocol of the NeuroCom

8 months

months

Diffusion tensor imaging

Caeyenberghs et al.

17 TBI and 14

Traumatic brain injury

14 years 5

10 years

(2010b)

controls

Tracking task (feedforward)

months

8 months

Diffusion tensor imaging

Caeyenberghs et al.

12 TBI and 17

Traumatic brain injury

14 years

10 years 6

(2012)

control

Diffusion tensor imaging and graph analyses

8 months

months

Caeyenberghs et al.,

12 TBI and 28

Traumatic brain injury (no focal lesions)

14 years 4

10 years

(in press)

controls

Resting-state fMRI

months

8 months

response to his/her sway such that the ankle joints did not bend

performing the dynamic tracking task, in which both spatial

in response to the sway, providing inaccurate proprioceptive

and temporal constraints had to be dealt with. As compared

input to the brain. Condition 5 was identical to condition 4

with the control children, the children with brain injury were

except that the eyes were now closed, such that only the vestib-

less successful in continuously keeping the cursor inside the

ular system was fully operational. Condition 6 was the same as

target, reflected in a shorter duration within the target, a larger

condition 4 except that the visual surround moved in response to distance (and variability of this distance) between the centers

the participant’s sway, and thus, both vision and proprioception

of cursor and target, and more feedback-based corrections

were compromised, leaving only the vestibular system as a reli-

(more velocity peaks per centimeter and more stops). The

able source. The subject’s sway was calculated from the maxi-

obtained results raised the question whether the structural

mum anterior and posterior centers of gravity displacements,

changes in the brain of TBI children are predictive of motor

occurring over the 20 s trial period. Our behavioral results

behavior deficits, as discussed in the next section.

revealed that the TBI group scored generally lower than the

control group on the SOT, especially in conditions where visual

and vestibular inputs must be relied upon to produce stability.

Structural Integrity of the Brain and Its Relation

The mean composite SOT score (average across all six condi-

to Motor Functioning in TBI

tions) also differed significantly between the TBI patients and the

controls. The lower scores of the subjects with TBI indicate

Traditional

imaging

techniques,

such

as

computerized

poorer balance (larger anterior/posterior body sway) than the

tomography and conventional magnetic resonance imaging

control subjects.

(MRI), have proved to be highly effective in identifying mac-

Second, eye–hand coordination was examined in two dif-

roscopic lesions, which is a necessary component in managing

ferent settings using the OASIS software and a WACOM digi-

acute TBI (Levin, 2003; Povlishock & Katz, 2005). However,

tizing tablet, allowing us to record, segment, and analyze pen

these techniques have marked limitations in assessing micro-

movements accurately (Caeyenberghs et al., 2009a, 2009b). In scopic lesions and cerebral physiology, such as those associ-

the static visuomotor task, a computerized version of the

ated with diffuse axonal injury (DAI), which is widespread

flower trail task of the Movement Assessment Battery for Chil-

damage to axons including white matter tracts and projections dren was used. Children traced a flower as accurately as possi- to the cortex. Diffusion tensor imaging (DTI), however, gener- ble with an electronic pen on a digitizing tablet and without ates images by taking advantage of the variability of both the speed constraints. In contrast, the dynamic task required faster speed and direction of water diffusion in vivo (Le Bihan et al., perceptual information processing and predictive movement 2001). DTI is based on the characteristics of myelin sheaths control. The children manually tracked a visible, accelerating and cell membranes of white matter tracts that restrict the target consisting of a circular configuration. The target acceler- movement of water molecules. As a result, water molecules ated when it was tracked successfully; otherwise, it decelerated move faster parallel to the major axis of nerve fibers rather to allow reentry. On the flower trail-tracing task, with only than perpendicular to them. This characteristic, which is spatial constraints, performance of children with brain injury referred to as anisotropic diffusion, is most commonly charac- was comparable to that of the control children. With the terized by a metric called fractional anisotropy (FA). It is deterexception of one dependent variable (number of errors), no

mined by several factors including the thickness of the myelin

significant group differences were found for the kinematic-

sheath and axons and the organization of the fibers and prop-

dependent variables. Thus, no striking differences were

erties of the intracellular and extracellular space around the

observed between groups in performing precise tracing. In

axon. FA ranges from 0 to 1, where 0 represents maximal

contrast, children with brain injury showed clear problems in

isotropic diffusion (e.g., free diffusion in all directions) and 1

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represents maximal anisotropic diffusion, that is, movement

various extents in young TBI patients and may have important

parallel to the major axis of a white matter tract. Isotropic

consequences for the final motor outcome of these patients.

diffusion of water in multiple directions is measured by the

The observed decrease of FA in our study was mediated by

mean diffusivity (MD) or ‘apparent diffusion coefficient.’ MD

the combined effects of AD and RD increases. Specifically, we
is often (but not always) negatively correlated with FA. Lower
found increased RD and AD in the TBI group for the whole
FA is often observed in TBI, especially in regions with diffuse
brain and for specific regions of interest, possibly reflecting
axonal injuries, and MD is higher in TBI (Huisman et al., 2004;
damage to both the myelin and axons (e.g., Arfanakis et al.,
Levin, 2003). While the summary parameters, FA and MD, are
2002; Boska et al., 2007; Concha et al., 2006; Mac Donald
commonly reported, the underlying eigenvalues hold addi-
et al., 2007). Kraus and colleagues (2007) also noted reduced
tional valuable information as they may be selectively affected
FA and elevated AD and RD in all of their 13 ROIs in chronic
with certain pathological processes (Song et al., 2002). Axial patients
sustaining moderate to severe TBI. In patients with
diffusivity (AD) reflects diffusivity parallel to axonal fibers.
mild TBI, FA was reduced in 3 of 13 ROIs (i.e., the corticospinal
Increases in AD are thought to reflect pathology of the axon
tract, sagittal stratum and superior longitudinal fasciculus),
itself, such as from trauma. Radial diffusivity (RD) reflects
whereas AD was only elevated in 2 of the ROIs (i.e., the sagittal

diffusivity perpendicular to axonal fibers and appears to be

stratum and superior longitudinal fasciculus). These findings

more strongly correlated with myelin abnormalities, either

suggest a continuum of widespread neural changes in moder-

dysmyelination or demyelination. In adults, DTI has been

ate to severe TBI affecting tissue organization, myelin, and

successfully employed in several patient populations, includ-

axonal integrity. Definite interpretation of these abnormalities

ing those with stroke (e.g., Sotak, 2002), multiple sclerosis

requires a comprehensive assessment of the white matter,

(e.g., Bammer et al., 2000; Filippi & Inglese, 2001; Fox, 2008;

which is the basis of the 'tractometry' philosophy introduced

Ge et al., 2005), epilepsy (e.g., Luat & Chugani, 2008; Widjaja

recently (de Santis et al., 2014). This method combines macro-

& Raybaud, 2008), Alzheimer's disease (e.g., Hess, 2009;

molecular measurements from optimized magnetization trans-

Stebbins & Murphy, 2009), and brain tumors (e.g., Mechtler,

fer imaging (Cercignani & Alexander, 2006), multicomponent

2009; Wieshmann et al., 2000). Most DTI studies in TBI have T2 species
from relaxometry (Deoni et al., 2008), and axonal

focussed on the adult population (for an excellent review, see density measurements from CHARMED (Assaf & Basser, 2005)

Hulkower et al., 2013).

along specific white matter pathways, providing a comprehen-

Our studies (see Table 1) used DTI-based maps for the

sive assessment of multiple microstructural metrics.

evaluation of various sensorimotor tracts and cerebral white

In view of this deterioration of white matter integrity in TBI

matter regions in an attempt to reveal the degree of structural

patients, the question emerges whether this structural discon-

brain damage (Caeyenberghs et al., 2010a, 2010b, 2011). We nection deficit has direct functional consequences. In our stud-

observed FA decreases in several regions and tracts in TBI

ies (Caeyenberghs et al., 2010a, 2010b, 2011), injury in both

patients, including the corpus callosum, brain stem, internal

efferent and afferent pathways was found to correlate with

capsule, corticospinal tract, cerebral peduncle, cerebellar

reduced motor performance in the TBI group, but not in the

peduncles, and anterior corona radiate, with several regions/

control group of typically developing participants. For exam-

tracts also demonstrating higher MD. There is some degree of

ple, the number of velocity peaks during the dynamic tracking

overlap between those brain regions that are particularly vul-
task was significantly correlated to mean FA in the anterior
nerable to injury in TBI and the structures believed to support
limb of the internal capsule (to a large extent occupied by the
motor function. For example, shearing injuries in TBI occur
corticospinal tract), indicating that less fluent tracking was
most commonly near the basal ganglia, superior cerebellar
related to lower FA. The equilibrium scores of the NeuroCom
peduncles, corpus callosum, internal capsule, and brain stem
SOT test (see earlier) was related to FA of the cerebellum, an
(Yeates, 2000). Moreover, decreased FA has been found in the important
structure for balance control. Hence, higher balance
TBI group in sensory cortex pathways, that is, posterior tha-
levels were associated with a higher white matter anisotropy.
lamic radiation and optic radiation. This suggests that white
Motor indices, though not fully investigated in the head injury
matter projections to or from sensory cortices rather than
literature, have previously been reported to be associated with
classical pyramidal motor tracts may play an important role
DTI measures in other disorders. For example, DTI metrics
in the pathophysiology of motor disability in some TBI chil-

are correlated with tests of upper-limb function in patients

dren. Compared to the motor system (corticospinal tract),

with congenital hemiplegia and chronic stroke patients

there has been limited DTI-based literature on the specific

(Bleyenheuft et al., 2007; Schaechter et al., 2009). Unfortu-

sensory pathways (Kamali et al., 2009). Few DTI studies have nately, studies correlating DTI parameters with kinematic mea-

assessed the sensory system in clinical conditions. For example,

sures of motor performance are scarce. The importance of the

in periventricular leukomalacia, DTI studies have demon-

changes in diffusivity in our study was also highlighted by the

strated decreased thalamocortical sensory connections, which

significant correlations between diffusivity and the motor

are responsible for the spasticity owing to impairment of inhib-

scores. Increases in MD, AD, and RD were associated with

itory function (Hoon et al., 2002, 2009; Nagae et al., 2007).

poor scores on the dynamic tracking task and the NeuroCom

This pattern of observed impairment of sensory WM pathways

balance task (see earlier). Additional analyses showed that the

corresponds well with our functional MRI (fMRI) study, indi-

FA of the cerebellum was the most critical DTI variable providcating that successful motor coordination in young TBI

ing maximal discriminability between TBI patients with poorer

patients is associated with enhanced activity in somatosensory

and better motor skills. These findings emphasize the vulnera-

regions relative to controls (see next paragraph). These findings

bility of the cerebellum to TBI and suggest the cerebellum as a

suggest that both sensory and motor pathways were affected to

target for therapeutic intervention.





It is important to note that no significant correlations were

basal ganglia, and anterior and posterior cerebellum during

found between the amount of global WM neuropathology and

the coordinated hand–foot movements.

motor deficits, whereas those between FA in individual ROIs

However, increased activation in brain regions was

and motor function did reach significance (Caeyenberghs

observed in the TBI group as compared with the control paret al., 2010a, 2010b). This observation suggests that injury to ticipants. No evidence was obtained for decreased activation

specific WM tracts and regions is probably responsible for the

relative to controls. More specifically, TBI children showed

motor deficits seen in patients with moderate to severe TBI. For

higher activation in the precuneus, which was hypothesized

example, FA of the optic radiation and cerebellar peduncles

to reflect increased attentional deployment for task perfor-

significantly contributed to the prediction of the visuomotor

mance. There is increasing agreement that this area is more

performance of the dynamic eye–hand coordination task

closely related to cognitive than to motor processes. The pre-

above and beyond whole-brain FA (Caeyenberghs et al.,

cuneus is involved in self-referential processing, imagery, and

2010a, 2010b). Thus, the specific motor deficits are often memory (Cavanna & Trimble, 2006), and its deactivation is

related to FA in task-specific WM structures. The absence of a

associated with anesthetic-induced loss of consciousness

relationship between whole-brain anisotropy and behavioral

(Alkire et al., 2008). These functional aspects can be explained

measures is inconsistent with previous studies (Kraus et al., on the basis of its high centrality in the cortical network

2007; Kumar et al., 2009), which have reported significant (Bullmore & Sporns, 2009; Gong et al., 2009; Hagmann

relationships between cognition and WM load. Previous work

et al., 2008; Iturria-Medina et al., 2007).

has also shown total WM FA to be correlated with clinical

Furthermore, additional activation was shown in posterior

markers of severity in a cohort of adolescents and adults with

cerebellar regions and somatosensory areas. The postcentral

TBI (ages 11–57) (Benson et al., 2007). Levin and colleagues

gyrus and inferior parietal lobule are known to be involved

(2008) also demonstrated a relationship between a composite in the integration of somatosensory information to guide

FA score, obtained 3 months after injury, and both clinical

motor actions (e.g., Ashe & Georgopoulos, 1994; Rizzolatti

severity of injury and concurrent global and specific cognitive

et al., 1998; Scott et al., 1997). The cerebellum is specifically

outcomes. However, cognitive functions rely on more wide-

known to be involved during ipsilateral coordination of differ-

spread cortical and subcortical networks than the motor sys-

ent effectors (Debaere et al., 2001, 2004; Heuninckx et al.,

tem, which is likely the reason why global WM load correlates
2005). Activation of the posterior cerebellum as compared
with cognitive function but not with motor function. Finally,
with the anterior cerebellum is more prominent with higher
these differences could also reflect the developmental stages of
task complexity levels and has previously been associated with
the subjects (children/adolescents vs. adults) and severity of
correction of timing adjustment errors. Overall, the findings of
the patient group (mild vs. moderate/severe).
this study suggest that TBI is associated with a shift along the
The aforementioned correlations between brain white mat-
continuum from automatic to more controlled information
ter structure and behavior, and more specifically between FA
processing for movement generation, as reflected by more
and motor deficits in a young TBI group, are of major interest
pronounced somatosensory processing and increased cogni-
for improving prediction of motor outcome in TBI patients
tive effort. Future studies are also needed to clarify both the
and may constitute a potential (bio)marker for therapeutic
short- and long-term effects of neural processing in TBI with

interventions.

respect to other motor tasks besides hand–foot coordination,

because of the possibility that TBI may result in a generalized

pattern of overactivation in the brain, rather than over-

activation specific to hand–foot coordination. We found

Brain Function and Compensatory Mechanisms

group differences in activation in some regions outside of the

in Young Brain-Injured Patients

motor network but were unable to determine if these areas are

recruited as compensatory mechanisms (that are directly asso-

Here, we focus on changes in brain function underlying motor

ciated with better motor task performance) or as part of a

behavior in young patients with TBI. We used task-related fMRI

generalized pattern of overactivation.

to compare brain activation patterns of TBI children with

Brain activation changes following adult TBI have been

controls during the performance of cyclical hand and foot

reported in previous functional imaging studies using simple

movements across different levels of coordinative complexity

motor tasks. In contrast to our work, Prigatano and colleagues

(Caeyenberghs et al., 2009a, 2009b). A TBI (N ¼ 9, only DAI (2004) found lower bilateral frontal activation on the Halstead patients) group and a control group (N ¼ 17) were scanned finger tapping test versus rest in seven severe chronic-phase while performing coordinated flexion–extension movements TBI patients as compared with eight healthy noninjured com- of the wrist and foot according to the ‘easy’ isodirectional and parison subjects, although this finding was only significant more ‘difficult’ nonisodirectional mode. Performance on the for right-handed tapping. Performance was matched across coordination tasks during scanning was similar between groups. Three of the patients had focal lesions by history. groups. The overall pattern of brain activation across the Lotze and colleagues (2006) showed also diminished fMRI groups was consistent with previous coordination studies signal change in the motor cortical network (contralateral using the same task. Comparing our results to findings of primary sensorimotor cortex, contralateral dorsal premotor Heuninckx et al. (2005, 2010) in young and older adults cortex, and SMA) in patients with moderate to severe TBI revealed activation in similar brain regions including the con-

(N ¼ 34) performing unilateral fist clenching motions. These

tralateral primary sensorimotor hand and foot areas, supple-

imaging studies with adults suggest that the neural circuitry

mentary motor area, supramarginal gyrus, temporal gyrus,

supporting motor control is altered after a brain injury, but it is

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unclear if this holds true for pediatric TBI and for other tasks.

future studies employing multiple conditions that vary in task

Furthermore, there is some inconsistency among the func-

difficulty are needed to distinguish them properly.

tional imaging studies in that some show evidence for

The finding that neural activation is altered following pedi-

overactivation, whereas others show underactivation in TBI.

atric TBI during coordination tasks has promising clinical

Our findings of overactivation are consistent with fMRI

implications. Persistent changes in neural mechanisms for

working memory studies in adults with TBI (Christodoulou years following childhood TBI suggest that motor function

et al., 2001; McAllister et al., 1999, 2001) and in children with should continue to be assessed in the chronic phase of TBI.

TBI. Newsome et al. (2007, 2008), Karunanayaka et al. (2007),

Kramer et al. (2008) each used fMRI to explore neural reorga-

nization after TBI in children and adolescents. It is difficult

Analyses of Structural and Functional Connectivity

to make direct comparisons between these studies because of

in Young Patients with TBI

differences in the experimental paradigms used. These vary

from working memory tasks (N-back task), attention tasks

Our previous discussed studies in TBI patients have related

(continuous performance task), interlimb coordination tasks

motor functioning to structural and functional properties of

(our study), to language tasks (verb generation paradigm). The

specific brain regions. However, the drawback of these regional

distributed networks involved in each task will vary, and thus,

analyses of brain structure and function is that they do not

brain activation differences in each experiment will differ.

reveal information about how the information is conveyed

However, taking this into account, there appears to be clear

across the different brain regions of a network (Hagmann
evidence in favor of a wider recruitment of brain regions in TBI
et al., 2008; Sporns et al., 2005).
children during a variety of tasks.
Resting-state fMRI (rs-fMRI) is a method of functional brain
Interestingly, Karunanayaka and colleagues (2007) found
imaging that relies on measuring low-frequency fluctuations
significant correlations for all subjects between the blood oxy-
(LFFs, $<0.1$ Hz) of BOLD signals and calculating functional
gen level-dependent (BOLD) signal activation and perfor-
connectivity between brain regions based on statistical depen-
mance on verbal fluency score, verbal IQ, and Glasgow Coma
dencies between intrinsic BOLD signal oscillations in these
Scale (GSC) score. Increased activation in many areas of the
regions (for a review, see Fox & Greicius, 2010). This (slightly)
language circuitry corresponded with poorer performance and
newer approach to functional imaging is still hobbled by a low
more severe injuries (lower GSC scores). In contrast, Kramer
SNR but has the distinct clinical advantages of (1) being easy to
et al. (2008) found that activation in the anterior cingulate, perform in
nonacademic imaging centers and (2) allowing

visual association areas (e.g., BA 19), and precuneus was pos-
for the collection of functional connectivity data in a much
itively related to task performance after controlling for group
broader spectrum of patients. We have collected rs-fMRI series
status. There is an inconsistency in these patterns of correla-
along with anatomical scans in patients with DAI and normally
tions across studies (and hence task paradigms), in that a
developing children (Caeyenberghs et al., in press). Further-
higher level of brain activation is not always associated with
more, we applied ‘functional connectivity density mapping,’ a
higher skill level or proficiency. Our small sample size and
voxel-wise data-driven method that calculates individual func-
restricted range of behavioral performance measures prohib-
tional connectivity maps to measure both short- (implicated in
ited an analysis of whether the relationship between task per-
functional specialization) and long-range (implicated in func-
formance and brain activation in specific regions changed
tional integration) FCDs (Tomasi & Volkow, 2010). Between-
depending on group status or injury severity. Future studies
group maps noted significantly decreased long-range FCD in

with larger samples are needed to examine group differences in

the DAI group in frontal and subcortical regions and signifi-

the relationship between activation level and behavioral per-

cantly increased short-range FCD in the frontal regions and left

formance in greater detail.

inferior parietal and cerebellar lobules. These findings suggest

Even though this ‘overactivation’ in young TBI patients has

that long-range connections may be more vulnerable to DAI

now been documented within the motor system, the underly-

than short-range connections. Moreover, higher values of

ing neural mechanisms are still unclear. McAllister and

short-range FCD may suggest adaptive mechanisms in the

colleagues (2001) suggested two possible neural mechanisms DAI group. Finally, lower balance levels on the SOT test in

to explain the observed neural overactivation following TBI:

patients with DAI were associated with a lower long-range FCD

differences in capacity or allocation of neural resources. Spe-

in left putamen and cerebellar vermis.

cifically, there may be a decrease in overall attentional capacity

In another study (Caeyenberghs et al., 2012), we used DTI-

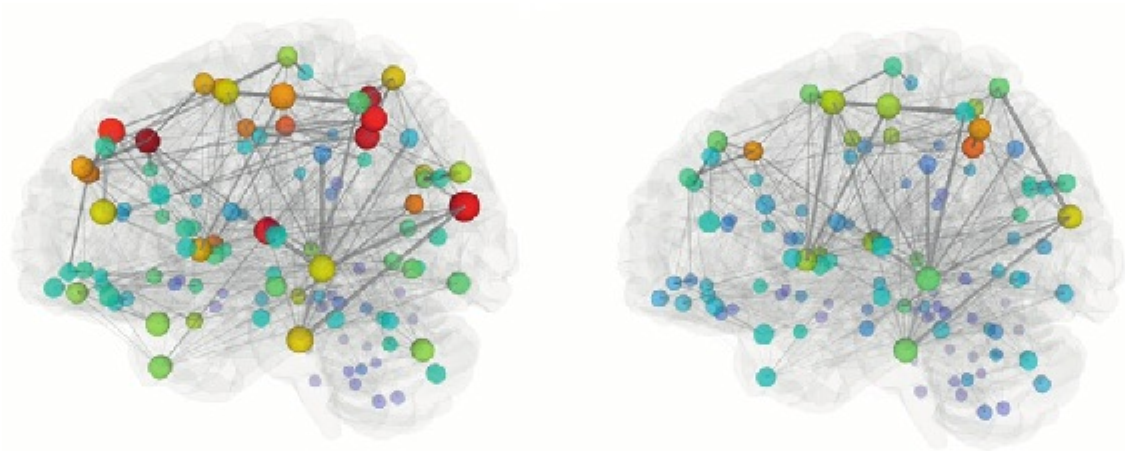
in young patients with TBI, rendering the coordination task

based fiber tractography to reconstruct the human brain white
more challenging, and hence more effortful, for this group to
matter networks of a group of young TBI patients and a group
perform at behavioral levels comparable to controls. Activation
of control participants, followed by a graph theoretical analy-
in the precuneus may be specifically augmented in young
sis. With graph theory, the brain can be represented in an
patients with TBI as a compensatory mechanism. Alternatively,
abstract way as a set of 'nodes,' defined by anatomical regions
subtle deficits in frontal executive functions may have rendered
in the cortex, and 'edges,' which reflect structural connection
the young patients with TBI less able to efficiently match
properties between these nodes. Using fiber tractography
available processing resources (which may be unimpaired) to
methods to define the node/edge characteristics, which are
the task demands. Consequently, they may overcommit pro-
typically represented by 'connectivity matrices,' such a graph
cessing resources to the coordination tasks without enhancing
theoretical network analysis provides a novel way to explore
performance. The neural mechanisms proposed by McAllister

topological and geometrical properties of brain networks,

and colleagues (2001) may differ only in very subtle ways, and including (1) global network metrics, such as small-worldness

*Brain Mapping: An Encyclopedic Reference, (* 2015), vol. 2, pp. 461-468



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Controls

TBI

improving diagnosis and treatment of patients with TBI. Future

studies will address the effects of specific training interventions

on brain structure, function, and connectivity, providing a

window into neuroplasticity in TBI patients. These insights

will provide a foundation for therapy to maximize sensorimotor recovery after brain damage.

See also: INTRODUCTION TO ACQUISITION METHODS:

Diffusion MRI; Obtaining Quantitative Information from fMRI.

Figure 1

Group differences in local efficiency. Left: controls. Right: TBI

patients. Size of the ROIs (spheres and nodes) represents the value of

local efficiency, and tube width of the lines (edges) represents the

number of tracts.

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(optimum between local specialization and global integra-

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nodes), clustering coefficient (the extent of interconnectivity

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among the neighbors of a specific node), and efficiency (how

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tion), a significant decrease of network connectivity was found.

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