

RELATIONS BETWEEN ATTENTIONAL STRUCTURE AND ATTENTIONAL
FUNCTION: UTILIZATION OF ALTERNATIVE STATISTICAL APPROACHES

A Thesis

Presented to

The Faculty of the Department

of Psychology

University of Houston

In Partial Fulfillment

Of the Requirements for the Degree of

Master of Arts

By

Paulina A. Kulesz

August, 2012

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ABSTRACT

Limited research findings regarding structure-function relations in the domain of attention may stem from problems in estimating these relations in small samples combined with data distributions that do not conform to the assumptions of the statistics used to estimate the relations. We examined the utility of using alternative statistics to estimate those relations. One hundred eleven children (82 spina bifida, 29 normal controls) were included to estimate behavior-behavior relations, and 61 children (43 spina bifida, 18 normal controls) were included to estimate structure-function relations. We used the Pearson's Correlation and four robust correlations: the Percentage Bend Correlation, the Winsorized Correlation, the Skipped Correlation using the Donoho-Gasko Median, and the Skipped Correlation using Minimum Volume Ellipsoid Estimator to investigate behavior-behavior and structure-function relations in the domain of attention. A bootstrap sampling process was used to compare performance of the five estimators in this field context. The results of the study suggest that utilization of robust methods to estimate structure-function and behavior-behavior relations can assist investigators when confronted with small samples and multivariate non-normal data. Furthermore, the similarity of estimates across correlational methods suggests that the lack of structure-function relations found in the literature is not easily attributed to violations of distributional assumptions.

Keywords: spina bifida, attention, outliers, robust correlations

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DEDICATION

*I dedicate this thesis to my beloved parents and
husband who always support me on the way to
success.*

Relations Between Attentional Structure and Attentional Function:

Utilization of Alternative Statistical Approaches

There was a broad interest in structure-function relations ever since people noticed that brain damage is accompanied by unusual behaviors. Our ancient ancestors believed that the brain is responsible for human behaviors. Their awareness of brain-behavior relations began research, which gradually enabled identification of specific brain areas involved in certain behaviors. As the time passed by, researchers were able to expand the knowledge about structure-function relations. Development of neuropsychological assessments and various neuroimaging techniques allowed more precise examination of brain areas and their associated functions. Despite significant progress in many areas of neuroscience, the study of structure-function relations in neurodevelopmental disorders has been hindered by small sample sizes, non-normal distributions, and inadequate behavioral assessments which may preclude precise identification of brain-behavior relationships. Better understanding of structure and function relations in the neurodevelopmental disorders may improve knowledge about behavioral and cognitive deficits as well as overall understanding of brain function in individuals with developmental deficiencies.

The present study focused on estimating structure-function relations in small clinical samples, where data might not be normally distributed. More specifically, the study investigated factors affecting the estimation of structure-function relations in the domain of attention in children with spina bifida and controls, and specifically examined the utility of using alternative statistics to estimate those relations.

The introduction is divided into four sections. To begin, the clinical manifestations of spina bifida, including general characteristics of physical, neural, and cognitive phenotypes

are described, followed by an overview of basic concepts of attention and attention processes, as well as attentional assets and deficits in spina bifida patients. Subsequently, factors affecting the estimation of the population correlation are reviewed, as well as alternative statistical approaches which have the potential to improve estimation of structure-function relations, and therefore strengthen inferences about variable relations.

Spina bifida

Spina bifida is a neural tube defect resulting from failure of closure of the neural folds, with a prevalence of approximately 19.3 per 100,000 live births in North America (Martin, Hamilton, Sutton, Ventura, Menacker, & Kirmeyer, 2006; Yi, Lindemann, Colligs, & Snowball, 2011). However, given the numerous factors potentially involved in the nature of the disorder, the incidence in other parts of the world might be different, with much higher prevalence in certain geographic locations (for instance China; Yi et al., 2011). Normally, the neural tube is formed by the fusion of the neural folds in the dorsal midline during the third and fourth week of gestation (Behramn, Kliegman, & Jenson, 2003). Spina bifida occurs when the neural tube formation is defective or incomplete. Depending on the severity, neural tissue, meninges, vertebrae, muscle and skin might be malformed (Sadler, 2000). Defective closure of the rostral neural folds, which normally fuse by the 23rd day of development, causes anencephaly (usually a fatal neural tube defect of the brain characterized by lack of the cerebral cortex), whereas failure of closure of the caudal neural folds, which normally fuse by the 27th day of development, leads to spina bifida (Behramn et al., 2003; Yi et al., 2011). Closed spinal defects are commonly classified as a spina bifida occulta, while opened neural tube defects are termed spina bifida cystica (Kaufman, 2004).

Forms of spina bifida. The most severe form of spina bifida, occurring in about 90% of cases, is meningocele in which the spinal cord, nerve roots, parenchyma and meninges herniate through the non-fused vertebral arches and skin forming a sac filled with neural tissue and fluid (Burmeister et al., 2005; Sadler, 2000). In meningocele, spinal abnormalities in the lumbosacral regions constitute at least 75% of cases (Behramn et al., 2003; Kaufman, 2004). In some cases, herniation is limited to meninges (spina bifida meningocele), which form a cystic cavity. Even though the neural tissue is not commonly a part of the defect in spina bifida meningocele, secondary protrusion of spinal cord is possible (Kaufman, 2004). Anterior meningoceles are commonly present in the sacral or thoracic regions; lateral meningoceles appear primarily in the thoracic regions, whereas posterior meningoceles predominately occur in the lumbar region (Kaufman, 2004). Spina bifida meningocele is less common than spina bifida meningocele (Lindsay & Bone, 2004).

Spina bifida occulta, with an incidence of approximately 1 per 1000 otherwise healthy individuals, is associated with the defective fusion of posterior vertebral arches in the lower lumbar/sacral regions (from L5 to S1) (Behramn et al., 2003; Kaufman, 2004; Sadler, 2000). Given that spina bifida occulta is associated with failure of closure of vertebral bodies, herniation of the neural tissue or meninges is not prevalent (Behramn et al., 2003).

Survival rate in spina bifida. Since neural tube defects, including spina bifida, are the second most common group of serious congenital disorders, investigation of the survival rate is an important issue. Appropriate treatment of spina bifida and its complications decreases mortality rate approximately to 10 – 15% (Behramn et al., 2003). Additionally, the mortality rate in spina bifida depends on severity of the symptoms and related complications (hydrocephalus, shunts), reaching approximately 1% per year of affected individuals

(Kaufman, 2004). Jenkinson et al. (2011) noted that only 46% of individuals with spina bifida reach age 35. However, progress in medical technology has significantly increased chances of children with spina bifida for surviving into adulthood. Yi et al. (2011) reported that the survival rate into adult life for children with spina bifida is up to 90%.

Roach, Short, and Saltzman (2011) recently reported information on common causes of death in spina bifida. Among the most common known causes of death before age 10, Roach et al. (2011) included general infection and hydrocephalus, whereas after age 10 they identified predominately infection (for instance sepsis), heart and kidney failure. However, the Roach et al. (2011) sample was limited in size ($n = 45$) suggesting that more research involving larger sample needs to be done to confirm these findings. Previously, Kaufman (2004) suggested that more severe dysfunction of the brainstem is associated with higher likelihood of mortality among neonates.

Etiology. Given the high mortality rates and severe consequences of brain malformations apparent in neural tube defects, there is a broad interest in the etiology of the disorder. Significant progress in etiological studies of neural tube defects, including spina bifida meningocele, has expanded knowledge about factors that might be involved in abnormal neurulation. Research findings have confirmed a multifactorial etiology focused on environmental and genetic factors (Fletcher & Dennis, 2009).

Among the environmental factors, which may play a significant role in the development of the disorder is nutritional deficiency. Previous studies have proven the importance of daily folic acid intake by women capable of or planning to become pregnant. With appropriate usage of folic acid dietary supplements, the likelihood of the neural tube defects decreases by at least 50% (Behramn et al., 2003; Fletcher & Dennis, 2009; Yi et al., 2011). In order to

lower the risk of neural tube defects, the United States Public Health Service suggests a daily consumption of 0.4 milligrams of folic acid for all women in the reproductive age (Kaufman, 2004; Sever, 1995).

Other environmental factors which have been linked with spina bifida meningocele are valproic acid (a chemical compound used in the treatment of epilepsy and bipolar disorder) and maternal occupation/maternal occupational exposure (Kaufman, 2004; Sever, 1995). There is evidence that valproic acid might be a putative teratogen, which significantly increases risk of spina bifida (Kaufman, 2004; Sever, 1995). Women who use anti-convulsants in the early stage of pregnancy have ten times higher risk of offspring with neural tube defects compared to the general population (Fletcher & Dennis, 2009). Moreover, Sever (1995) suggests that some maternal occupations such as nursing involving exposure to radiation, mercury, anesthetic gases, and solvents might increase the risk of neural tube defects. However, more research needs to be done in order to confirm the findings.

The role of genetic factors in neural tube defects, including spina bifida meningocele, has been shown in the familial history of the disorder. The risk of spina bifida increases with the number of affected children in the particular family. In other words, when one child is affected, the other has a 2 to 5% chance of being affected, and when two children are affected the third one a 10 to 15% chances for the development of the disorder (Kaufman, 2004).

It has been suggested that genes involved in folate and glucose metabolism might be involved in the development of the neural tube defects (Behramn et al., 2003). Women, who have problems with the metabolism of folic acid and/or have diabetes might be at higher risk of having the offspring with neural tube defects. Gene mutations affecting the metabolism of

folate or glucose have a higher prevalence among Hispanics and Caucasians (Fletcher & Dennis, 2009).

Future research will surely improve understanding of neural tube defects, such as spina bifida and meningomyelocele, and their etiology. There is growing evidence that environmental and genetic factors might be responsible for the underdevelopment of the posterior fossa, which has important consequences for the developing infra- and supratentorial regions of the brain (Juranek & Salman, 2010).

A detailed review of the etiology of neural tube defects is beyond the scope of the present study. We turn now to a description of the physical, neural, and cognitive phenotype of spina bifida.

Physical phenotype. Spina bifida meningomyelocele is a pathology of the skeleton and nervous system that also involves abnormalities in the skin and genitourinary tracts (Behramn et al., 2003). The severity of conditions associated with spina bifida meningomyelocele depends on the level of spinal lesions.

Individuals with the meningomyelocele spinal lesions at the higher level commonly have more orthopedic and urological problems compared to persons with lower spinal lesions (Fletcher et al., 2005). As with most spinal cord lesions, patients having upper lumbar lesions are more likely to have severe consequences with regards to mobility than patients with sacral lesions. This difference in anatomical location results in requiring a wheelchair versus being able to walk independently (Kaufman, 2004). The location of the lesions can be clearly evident based on the symptoms and clinical manifestations that occur. Lesions in the lower sacral area cause bladder and bowel dysfunction due to the loss of sensation in the perineal area, although there are no effects on the motility of the intestines or micturition. Patients

with midlumbar lesions may present flaccid paralysis of the lower extremities, loss of tendon reflexes, orthopedic disorders such as clubfoot and hip dysplasia, and loss of nociception and tactile sensation in the lower extremities (Behramn et al., 2003).

Continuous progress in medical knowledge and technology has significantly improved the quality of life of patients with spina bifida meningocele. Various medical procedures have been implemented for treating the orthopedic and urological complications in those patients with some degree of success (Lindsay & Bone, 2004).

Neural phenotype. Past findings demonstrated differences within the neural phenotype of patients with spina bifida meningocele having variations in cephalic volume, form, and general appearance of abnormal structures (Juranek & Salman, 2010). Common manifestations include the cranial, subcortical, and cortical malformations (Juranek & Salman, 2010).

Chiari II malformation highly prevalent in spina bifida meningocele is pathology of cerebellum and brainstem (Juranek & Salman, 2010). In Chiari II malformations the posterior fossa does not develop properly, resulting in the smaller than normal size. Because of the decreased size of the posterior fossa, brain structures are compressed.

At least 80% of individuals with spina bifida meningocele and Chiari II malformation have hydrocephalus, which is a consequence of a decreased posterior fossa (Behramn et al., 2003; Burmeister et al., 2005). Hydrocephalus is associated with enlarged ventricles and obstruction of cerebral spinal fluid flow due to a displaced brainstem and cerebellum (crowding of the foramen magnum; Juranek & Salman, 2010). The risk of hydrocephalus is higher in patients with upper spinal lesions (Behramn et al., 2003).

Rhombencephalic abnormalities are present in roughly one fifth of patients with Chiari II malformation and hydrocephalus (Behramn et al., 2003; Kaufman, 2004). Symptoms differ within various age groups and develop the most rapidly in the earliest period of life. In the first year of life dysphagia, aspiration pneumonia, and stridor are the main complications due to brainstem malfunctions (Kaufman, 2004). Later childhood is associated with increased frequency of aspiration, and weakness of the extremities that can progress into adolescence as spasticity and sensory defects (Kaufman, 2004). It is worth noting that the above symptoms may also be a consequence of shunt dysfunction or hydrocephalus (Kaufman, 2004).

Cerebellum and Brainstem. The cerebellum and surrounding structures are significantly affected in spina bifida, largely as a result of the diminished size of the posterior fossa. As a consequence of the posterior fossa being too small, the developing cerebellum does not have enough room to grow and protrudes through the foramen magnum compressing other structures. The inferior vermis of the cerebellum is compressed with a downward force from the tentorium cerebelli which dislocates it inferiorly into the foramen magnum, whereas the superior vermis herniates upward (Brant & Helms, 1999; Juranek & Salman, 2010). Cerebellar dislocation and compression may occur from C1 to T1 levels (Kaufman, 2004).

Earlier quantitative studies provide evidence for smaller cerebellar volume and/or gradual deterioration of the structure among individuals with spina bifida meningocele (Juranek & Salman, 2010). Juranek, Dennis, Cirino, El-Messidi, and Fletcher (2010) demonstrated that smaller cerebellar volume was not uniform throughout the cerebellum. Individuals with spina bifida meningocele had decreased volume in posterior-inferior subdivision of the cerebellum when compared to typically developing individuals. However, their anterior lobe

was significantly larger when compared with the control group. Dennis et al. (2004) found that reduction in the cerebellar volume is associated with the level of the spinal lesion. Similar findings were presented by Fletcher et al. (2005), who found smaller cerebellar volume in patients with upper spinal lesions.

The diminutive posterior fossa also alters development of the midbrain. The “beaking” of the tectum characterized by a distorted and stretched (posteriorly and inferiorly) appearance of the structure is present in 75% of the Chiari II malformation cases (Behramn et al., 2003; Juranek & Salman, 2010). Fletcher et al. (2005) found that children with upper spinal lesions had greater malformations of the tectum compare to the individuals with lower spinal lesions.

Due to small posterior fossa and cerebellar compression, the pons and medulla are compressed inferiorly and may extend to the foramen magnum or spinal cord at the cervical level (Brant & Helms, 1999), whereas the cervicomedullary junction might be kinked (Kaufman, 2004).

Corpus callosum. The supratentorial region of the brain is associated with malformations of the following structures: the corpus callosum, the thalamic massa intermedia, and the cerebral cortex (Kaufman, 2004; Miller, Widjaja, Blaser, Dennis, Raybaud, 2008). Abnormal development of the corpus callosum, which may involve agenesis, partial dysgenesis, or/and decreased volume, is present in 70 to 90% of individuals with spina bifida meningocele (Juranek & Salman, 2010). Thinning of the corpus callosum is considered to be a consequence of hydrocephalus (Juranek et al., 2008).

Hannay, Dennis Kramer, Blaser, Fletcher (2009) have reported different morphological patterns of the corpus callosum along its rostrocaudal axis. In the study involving 193 patients with spina bifida meningocele 26 corpus callosum regional patterns were

distinguished. A Partial agenesis of the corpus callosum in rostrum, splenium or both of the regions was present in half of children, while properly formed corpus callosum was noted in only 4% of children. Fletcher et al. (2005) found that the splenium varies in individuals with upper spinal lesions compared to patients with lower spinal lesions. More specifically, those with upper spinal lesions have more abnormalities in that region. Similarly, Juranek & Salman (2010) noted that the splenium is most affected by dysmorphology of the corpus callosum. It is noteworthy that the anteriorly located genu of the corpus callosum has normal morphology.

Cortex. Underdevelopment of other posteriorly located structures is also present in the cerebral cortex. It has been suggested that cortical abnormalities are related to the obstruction of the cerebral spinal fluid flow (Juranek et al., 2008). Malformations of the cerebellum and hindbrain lead to the abnormal flow of cerebral spinal fluid at the level of the fourth ventricle resulting in hydrocephalus (Juranek et al., 2008). The obstruction of posteriorly located brain structures due to the abnormal flow of cerebral spinal fluid might be accountable for thinning of the cortex in more posterior temporal, parietal, and occipital (Burmeister et al., 2005; Juranek et al., 2008).

In recent quantitative studies volumetric changes within the cerebral cortex (especially in the posterior regions of the brain) were found. Fletcher et al. (2005) found a decrease in the grey and white matter volumes of cerebrum that lie posterior to the genu of the corpus callosum. The reduction in the grey and white matter volumes was greater for individuals with the upper level spinal lesions. Juranek et al. (2008) found decreased volumes in temporal, parietal, cingulate, and occipital regions in individuals with spina bifida meningocele. However, the same pattern was not found for the frontal region, which

had similar volume in individuals with spina bifida and controls. Moreover, spina bifida patients have decreased thickness of the posterior cortex, and increased thickness of the frontal regions. Additionally, in Miller et al. (2008) cortex stenogyria, characterized by occurrence of undersized compacted gyri with shallow sulci, was observed in 73% of patients. The stenogyria was mostly present in the posterior surface of the hemispheres.

Underdevelopment of posterior structures and overdevelopment of anterior structures has important implications for the cognitive functioning depending on posterior and anterior brain networks. Heterogeneous development of the brain structures is associated with specific cognitive strengths and weaknesses in children with spina bifida meningocele.

Cognitive phenotype. The characteristic cognitive phenotype apparent in spina bifida results from the neural phenotype, which is affected by genetic and environmental factors (Dennis, Landry, Barnes, Fletcher, 2006). Abnormalities of infra- and supra-tentorial brain regions, primarily related to the Chiari II malformation, lead to impaired development of cognitive functions associated with timing, movement, and attention. Dennis et al. (2006) report that deficient timing, movement, and attention affect the cognitive abilities associated with generating information (assembled processing), but do not affect to the same degree cognitive skills involving classification of information (associative processing). Therefore, due to the variability of outcomes associated with brain malformations, the cognitive phenotype of individuals with spina bifida can be characterized in terms of intact and impaired functions. Dennis & Barnes (2010) suggest that the inclusion of assets and deficits in the cognitive phenotype enables a full description of a complex pattern of cognitive function that is apparent in spina bifida. Moreover, Dennis et al. (2006) postulate that core deficits involving timing, movement, and attention have some common characteristics. More

specifically, they begin in infancy and continue through adulthood. The impairments are the consequence of brain malformations, and are similar to the cognitive dysfunctions experienced by individuals with lesions acquired in adulthood that are located in corresponding brain areas (Dennis et al., 2006).

Timing. Timing is a dysfunction occurring in individuals with spina bifida meningocele, which affects various temporal operations associated with motor regulation and movement synchronization (Dennis et al., 2006). In the typically developed brain, the cerebellum plays an important role in motor and perceptual timing. Due to cerebellar malformations in spina bifida meningocele, sensation-movement synchrony and limb coordination are impaired (Dennis et al., 2004). Dennis et al. (2004) found that individuals with spina bifida have more problems with perception of duration and motor timing when compared with the control group. They experience difficulties with producing rhythms based on the internally generated pace. However, their production of synchronous rhythms is intact (Dennis & Barnes, 2010). Moreover, Dennis et al. (2004) found that deficits in duration perception and motor timing are related to the cerebellar volumes in patients with spina bifida, confirming the existence of structure-function relations. Specifically, the authors found positive correlations between lateral cerebellar cerebral spinal fluid volume and duration perception, as well as between motor timing and cerebellar volumes. Timing deficits significantly affect everyday functioning of individuals with spina bifida. Dennis et al. (2006) suggest that deficient timing impairs temporal coordination between perception and movement. Therefore, patients with spina bifida meningocele have problems with synchronizing sensation and movement, which is necessary to perform many motor tasks (Dennis et al., 2006).

From a research standpoint, knowledge about timing deficits in spina bifida has important implications for construction of assessments, which should be accurately adjusted to the abilities of patients. Evaluation of cognitive skills should account for the temporal limitations of patients with spina bifida meningocele. Therefore, a better understanding of those core deficits allows for more precise examination of structure-function relations.

Movement. Movement is a deficit apparent in spina bifida meningocele, characterized by impaired motor functioning of limbs and eyes (Dennis et al., 2006). Due to movement deficits individuals with spina bifida meningocele experience decreased strength, speed, and quality of movement (Juranek & Salman, 2010). The severity of the deficient movement performance is directly related to cerebellar and midbrain malformations. Movement planning and posture, as well as limb and head movements are controlled by the cerebellum (Martin, 2003). Eye movements are controlled by the cerebellum and the superior colliculus (Martin, 2003). Therefore, abnormalities of those brain structures affect motor control. Moreover, motor deficiency is also indirectly associated with the level of spinal lesion. Fletcher et al. (2005) found that the reduction in the grey matter volume of medial and lateral cerebellar regions, as well as the midbrain was greater in the individuals with upper spinal lesions. Therefore, movement deficits are more severe in patients with upper spinal lesions when compared to individuals with lower spinal lesions (Dennis et al., 2006).

Motor exploration is a requirement for orienting one's self within the physical environment. Mapping the spatial positions that result from previously executed motor movements can be used to predict, improve and plan accurate motor movements by comparing the intended results with the actual outcomes. Dennis et al. (2006) noted that

individuals with spina bifida meningocele have problems with motor planning, which could be explained by the decreased motor exploration seen in those patients. Additionally, as a consequence of limited exploration, individuals with spina bifida experience difficulties with learning from the environment, which relates to assembled processing (Dennis et al., 2006). However, patients with spina bifida have an intact ability of learning based on trial and error, which is closely related to associative processing (Fletcher, Ostermaier, Cirino, Dennis, 2008). Fletcher et al. (2008) report that learning based on the correction of errors in individuals with spina bifida meningocele is comparable with typically developing persons. Therefore, motor learning associated with motor adaptation of extremities and eyes is considered to be an asset in spina bifida meningocele (Dennis et al., 2006).

Continued research progress will help to provide a better understanding of the strengths and weaknesses in spina bifida within the movement domain. Similarly, continued, detailed exploration of assets and deficits will improve our understanding of cognitive functions in spina bifida, which in turn will allow for more comprehensive examination of the limitations associated with specific brain abnormalities in spina bifida. However, further investigation of the timing and movement deficits is beyond the scope of the present study. Consequently, we turn now to a description of the attentional phenotype of spina bifida.

Attention

In order to fully understand the attentional phenotype in spina bifida meningocele, a description of attention and attentional processes is needed beforehand. In a broad sense, attention is an integrated system that controls the processing of information in the complex environment by orienting towards selected stimuli, and maintaining focus on the specific

goals for a longer period of time. Attention function involves a wide range of brain structures which ensure appropriate processing of various stimuli (Posner & Petersen, 1990).

Types of attention. Three primary types of attention can be distinguished depending on their function and neural basis: selective attention, divided attention and sustained attention. Shulman, Astafiev, Corbetta (2004) note that selective attention can be understood as a cognitive process responsible for focusing on unexpected or internally motivated stimuli. The selection of stimuli enables their further processing, and is associated with a distribution and allocation of the limited resources. Selected stimuli occurring in the attended location are processed more rapidly (for the first 150 ms) compared to stimuli presented in the unattended locations (Posner & Petersen, 1990). The processing of prioritized stimuli requires focusing attention on them, while ignoring other stimuli accessible at the same time. Despite active processing of selected stimuli other stimuli do not remain completely unprocessed (Ward, 2004). Negative priming, in which ignored stimuli influence upcoming responses, confirms partial processing of unattended stimuli (Ward, 2004). Selection of information involves the attentional control, which allows attending important or interesting stimuli at the moment. In other words, the control of attention is a conscious process, which enables individuals to concentrate on certain activities.

It is noteworthy that processes involved in selective attention are similar for different modalities. However, the mechanisms involved in receiving sensory inputs differ depending on the sensory modality (Posner, Sheese, Odludas, & Tang, 2006). In the past, researchers examined both auditory and visual attention. Nevertheless, since 1970 the majority of the studies concerning attention have focused on the visual domain (Ward, 2004).

Divided attention is an ability to process several stimuli at once (Ward, 2004). Divided attention helps in processing highly complex environments. Depending on the complexity of stimuli, a different number of stimuli can be processed simultaneously. With more demanding tasks less stimuli can be processed at the moment. Additionally, the quality of tasks performed at the same time is worse compared to the quality of individually performed tasks (dual task deficit) (Ward, 2004). Furthermore, the interference is greater when simultaneous tasks involve the same modality or similar cognitive processes, for instance both tasks require storing information in the working memory (Ward, 2004). Increased cognitive load associated with simultaneous processing requires activation of the additional brain area - the right inferior frontal gyrus (Ward, 2004). Therefore, the cost of simultaneous processing of stimuli is greater compared to processing of an individual stimulus.

Sustained attention refers to an ability to maintain a prolonged and “efficient level of responding to demanding tasks” (Ward, 2004, s. 133). In other words, sustained attention is related to focusing on certain stimuli over extended periods of time. Furthermore, sustained attention helps in continuously monitoring the environment in order to direct and focus cognitive processes on occurring stimuli. Sustained attention is especially crucial in monotonous tasks, in which individuals do not receive much stimulation. In other words, sustained attention is particularly useful when there is not enough external stimulation, which could help an individual in staying focused on the task in order to react on random and infrequently occurring stimuli (Sarter, Givens, & Bruno, 2000). It is noteworthy that sustained attention is oftentimes confused with alertness. However, alertness and sustained attention refer to different cognitive processes, and therefore those terms should not be treated as substitutes for each other.

Attention networks. According to Posner and Petersen (1990) there are three interrelated attentional networks (orienting, alerting, and executive control) which allow information processing. Those attention networks play an important role in supporting other cognitive processes (Posner & Petersen, 1990; Rueda et al., 2004).

Orienting is closely related to selectivity. Klein (2004) suggests that the visual selectivity of stimuli depends on: (1) reorienting eye and/or head movements towards selected stimuli (overt orienting), or (2) internal shifts of attention, which are not observable, since they do not involve eye and body movements (covert orienting). Overt and covert orienting depend on two types of stimulation - external stimulation commonly resulting in automatic shifts (exogenous), and internal stimulation resulting in voluntary shifts (endogenous), respectively (Klein, 2004). It has been proposed that covert orienting involves the superior parietal cortex (Posner, Walker, Friedrich, & Rafal, 1984), the temporoparietal junction, the frontal eye fields, the pulvinar nucleus (thalamus), and the superior colliculus (Jonhson et al., 2008; Posner & Petersen, 1990), which are responsible for the different functions associated with covert orienting. According to Posner et al. (1984) covert visual orienting is related to three processes – engaging, disengaging, and shifting/moving attention. The superior partial cortex is associated with disengaging attention, whereas the lateral pulvinar is involved in engaging attention. Speed of attentional shifts depends on the superior colliculus. Patients with an impaired superior colliculus are not able to move their gaze into a certain direction. However, they are capable of shifting attention towards that direction at a slower than normal pace. In other words, patients with damaged superior colliculus are still able to shift attention, but they do that more slowly when compared to normal controls. Furthermore, Posner & Petersen (1990) suggested that shifting attention towards stimuli (targets) is associated with

mental preparation to shift attention (the covert shift), and observable saccadic eye movements (the overt shift). Covert orienting preceding overt orienting, prepares individuals to physically change their focus by redirecting eyes towards a selected visual field. According to the premotor theory of attention (Castiello & Paine, 2002), covert attentional shifts are most likely associated with the same brain regions as overt attentional shifts, which involve eye and arm movements. To summarize, orienting is possible due to disengaging from the present stimulus (the superior parietal cortex), then shifting into a new location (the superior colliculus), and engaging into a new location (the pulvinar; Posner & Petersen, 1990).

Alertness is associated with an ability to react upon upcoming and unforeseen stimuli. More specifically, alertness is related to being vigilant, cautious and prompt in order to respond to unexpected stimuli (for instance danger or emergency). It has been proposed that maintaining an alert state is associated with the right cerebral hemisphere (Posner et al., 2006). More specifically, it has been suggested that the posterior cortex of the right hemisphere, as well as the thalamus are related to maintaining an alert state (Coull, Frith, Frackowiak, & Grasby, 1996; Fan, McCandliss, Sommer, Raz, & Posner, 2002; Posner & Petersen, 1990). Additionally, there has been some evidence suggesting an important role of the locus coeruleus (brainstem), which is controlled by the frontal and parietal regions, in non-stimulus-driven alertness (Posner et al., 2006).

The executive control of attention is often investigated utilizing tasks that require resolution of conflict between interfering stimuli (Fan, et al., 2002). Conflict resolution might be interpreted as an ability to respond to contradicting stimuli by resolving occurring between them inconsistency. Therefore, conflict resolution is associated with decision-

making and self-regulation. Previous studies have shown that conflict resolution is controlled by the dorsolateral prefrontal cortex and the anterior cingulate cortex (Danckert et al., 2000; Posner & Petersen, 1990; Rueda et al., 2004).

Assets and deficits of attention in spina bifida. Similarly to timing and movement, the attention phenotype of individuals with spina bifida can be characterized in terms of strengths and weaknesses. Despite rather average intelligence, individuals with spina bifida exhibit impairment of certain cognitive functions (Brewer, Fletcher, Hiscock, & Davidson, 2001; Dennis, Sinopoli, Fletcher, & Schachar, 2008). Broadly speaking, patients with spina bifida meningomyelocele experience difficulties with covert orienting reflected by accurate but slower attentional shifts, and greater disengagement cost to exogenous stimuli (Dennis et al., 2008). However, they do not have as many problems with activities involving sustained attention and conflict resolution (Burmeister et al., 2005; Dennis et al., 2008).

The characteristic pattern of attention assets and deficits is related to brain areas responsible for those cognitive functions. The anterior network involved in the top-down processes (cognitive response control) is mostly controlled by frontoparietal areas of the brain, whereas the posterior network involved in the bottom-up processes (stimulus response) is predominately controlled by the midbrain (the superior colliculus) and posterior parietal regions (Posner & Petersen, 1990; Sarter et al., 2000). Posner and Petersen (1990) suggest that sustained attention, executive control, and response inhibition are associated with the anterior brain network, whereas orienting and attention shifts involve the posterior brain network.

Due to impaired function of the posterior system resulting from abnormalities of posterior brain regions related to hydrocephalus (Rose & Holmbeck, 2007), individuals with spina

bifida have problems with orienting, disengaging and shifting attention. In the study conducted by Rose and Holmbeck (2007) adolescents with spina bifida had an intact ability to sustain attention and impaired ability of focused visual attention. However, the authors suggested that their obtained results could have reflected their use of different measures to assess sustained attention skills (Behavior Rating Inventory of Executive Function, BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000) and focused visual attention abilities (Cognitive Assessment System, CAS; Naglieri & Das, 1997).

Dennis et al. (2005a) using a variation of Posner's paradigm task, found that children with spina bifida meningomyelocele have problems with covert orienting. Specifically, covert orienting to exogenous and endogenous stimuli was slower in spina bifida patients when compared with typically developing children. Moreover, children with spina bifida had more problems with disengaging from exogenous stimuli. However, they did not experience difficulties with disengaging from endogenous stimuli involving the anterior attention network. Dennis et al. (2005a) suggest that orienting deficits might be a consequence of abnormalities found in the midbrain (tectal beaking) and right posterior cortex, which are associated with the posterior network. Similar findings were presented by Taylor, Landry, Barnes, Swank, Cohen (2010), who found that infants with spina bifida required more time in order to disengage from exogenous stimulus (a blinking light) and shift their attention towards more cognitively interesting stimulus (a face) when compared to typically developing infants. Moreover, the authors found that shifting attention from exogenous to endogenous stimuli was related to motor performance. Longer reaction times were noted in infants with worse motor performance. Taylor et al. (2010) suggested that the relationship between motor performance and attention function might be related to parietal lobe function,

which is involved in both orienting attention and visual-motor function. Vinck, Mullart, Rotteveel, Maassen (2009) also found that attention performance might be related to motor performance. More specifically, children with spina bifida meningocele performed worse on the focused attention task involving motor performance (Symbol Searching and Coding subtest of Wechsler Intelligence Scale for Children, WISC-III; Wechsler, 2002) than spina bifida children, who did not have problems with motor functioning. In contrast, on the computerized task (Amsterdam Neuropsychological Tasks, ANT; de Sonneville, 2003) the group differences were less pronounced. However, the overall small sample sizes in the spina bifida meningocele and spina bifida groups ($n = 31$, $n = 20$, respectively) necessitates that the results be interpreted with caution. It is noteworthy, that research findings about motor functioning and attention performance relations are not consistent. Some researchers (Fletcher & Dennis, 2009) argue that attention performance is related to motor skills whereas others (Brewer et al., 2001) postulate that motor function does not play a significant role in attention function.

The other problem with studying attention function in spina bifida patients arises from the potentially confounding role of hydrocephalus, which leads to the abnormal development of posteriorly located structures. Iddon, Morgan, Loveday, Sahakian, Pickard (2004) found that patients with congenital or acquired hydrocephalus obtained lower scores on the attention set-shifting task than a control group and a group consisting of patients with spina bifida without hydrocephalus. However, in a recent study Swartwout et al. (2008) found that hydrocephalus did not explain the distinct attentional phenotype of spina bifida meningocele patients. Specifically, children with spina bifida meningocele had more attention problems compared to children with aqueductal stenosis (a congenital birth

disease, which produces hydrocephalus due to the narrowed cerebral aqueduct connecting the third and fourth ventricles). Swartwout et al. (2008) suggest that cognitive dysfunction of spina bifida meningomyelocele patients might be related to greater abnormalities of the posterior network, which is not as deteriorated in patients with hydrocephalus of different etiology. Additionally, Mataro et al. (2000) suggest that impaired cognitive functioning might be related to the treatment of hydrocephalus. Specifically, the authors found that shunt placement required to regulate the cerebral spinal fluid flow in spina bifida meningomyelocele patients, leads to improvement of neuropsychological functioning, including attention. However, due to small sample size ($n = 23$) the findings need further verification. To summarize, the findings discussed above provide evidence for the possibility of a differential role of hydrocephalus in attention functions. Further research may help in better understanding of the relation between hydrocephalus and attention function.

Despite deficits with orienting, disengaging, and shifting attention, individuals with spina bifida meningomyelocele have preserved ability to sustain attention. Swartwout et al. (2008) found that children with spina bifida perform similarly to typically developing children on the sustained attention task (Vigilance Task in Gordon Diagnostic System, GDS; Gordon, 1983). The overall performance across all trials was comparable in both groups. However, children with spina bifida had longer reaction times and committed more errors of omission and commission. Swartwout et al. (2008) suggest that those findings may indicate impairment of certain cognitive functions associated with the anterior system. Similar results were presented by Taylor et al. (2010), who found that spina bifida infants do not differ from typically developing infants in terms of sustained attention skills. Specifically, they were able to concentrate on the interesting stimulus over longer period of time.

Difficulties with accurate measurement and estimation of structure-function relations in patients with spina bifida limit findings. Further investigation of brain-behavior relations using appropriate assessments and statistical measures may improve understanding of neural networks involved in attentional processes of spina bifida patients. Importantly, a better evaluation of the structure-function relationships in spina bifida would enrich knowledge about brain development in neurodevelopmental disorders and may provide information about possible compensatory mechanisms occurring in the malformed brain. In other words, investigation of the structure-function relationships in spina bifida could help in explaining how the abnormally developed brain functions with certain structural deficits. Moreover, a better understanding of brain-behavior relations could result in the development and implementation of more efficient interventions targeting the attentional deficits in spina bifida.

Spina bifida and ADHD. The Attention Deficit Hyperactivity Disorder (ADHD) might be broadly described as a psychiatric disorder involving impairments of attention and inhibitory control. According to the Diagnostic and Statistical Manual of Mental Disorders (4th ed. [*DSM-IV*]; American Psychiatric Association, 1994), three subtypes of ADHD based on the predominant pattern of symptoms can be distinguished. The combined type is characterized by the equal amount of inattentive and hyperactive-impulsive symptoms. The predominantly inattentive type is present when attentional deficits are the dominant symptoms, whereas the predominantly hyperactive-impulsive type occurs when hyperactive-impulsive deficits are dominant.

Due to attention deficits, individuals with spina bifida are at higher risk of ADHD. In the study conducted by Ammerman et al. (1998), 18 out of 54 (33%) children and adolescents

with spina bifida met the DSM-IV criteria for ADHD diagnosed using Child Symptom Inventory (CSI; Gadow and Sprafkin, 1987). Furthermore, within the ADHD subgroup symptoms associated with impaired attention were more common compared to symptoms involving hyperactive and impulsive behavior. Similar findings were presented by Burmeister et al. (2005), who found that one third of children with spina bifida meningocele, met DSM-IV criteria for ADHD diagnosed using Swanson Nolan Achenbach Pelham-IV (SNAP-IV; Swanson, 1992). Within the ADHD group two thirds of spina bifida meningocele patients were categorized as predominately inattentive type, whereas remaining individuals were classified as predominately impulsive-hyperactive type with one exception of combined type. Moreover, the percentage of spina bifida patients with ADHD (33%) was significantly greater than the incidence of ADHD in a general population (17%) (Burmeister et al., 2005).

Higher prevalence of symptoms related to attention deficits in individuals with spina bifida might be a consequence of motor impairments, which preclude overactive and impulsive behaviors (Ammerman et al., 1998). Burmeister et al. (2005) noted that individuals with spina bifida experienced similar difficulties to those demonstrated by persons with ADHD. Specifically, they have problems with multitasking and are easily distracted. However, the overall pattern of attention skills was different in both groups. In spina bifida patients sustained attention abilities were intact, while focusing and shifting attention was impaired. The opposite was true for the ADHD individuals. Therefore, it is also possible that predominance of attention deficits is a result of the distinct cognitive phenotype recognized in spina bifida patients, where higher incidence of ADHD in spina bifida patients might be

interpreted as an additional confirmation of the persistent attention impairment in that disorder (Ammerman et al., 1998).

In order to fully explain higher prevalence of ADHD in spina bifida patients more research needs to be done. Better understanding of neural networks involved in both disorders can help in further exploration of structure-function relations.

Current research. Research findings regarding brain-behavior relations in spina bifida meningomyelocele are very limited. Correlations between structural brain changes in spina bifida and cognitive phenotype, specifically attentional phenotype, are not well understood. The only study examining relations between attention function and brain structures in spina bifida meningomyelocele patients was conducted by Dennis and colleagues (2005a), who found that spina bifida patients with the malformed superior colliculus and posterior volume loss had slower attentional shifts, and higher disengagement cost (in other words, their responses to a target were slower when a cue suggested a wrong location of an upcoming target compared to a condition, in which a cue correctly indicated location of the upcoming target; Dennis et al., 2005a) to exogenous (but not endogenous) stimuli than typically developing children and children with spina bifida meningomyelocele without tectal beaking (Dennis et al., 2005a). Limited research findings with regards to structure-function relations in spina bifida population might be a consequence of problems associated with statistical estimation of those relations. Consequently, it is important to investigate factors affecting the study of structure-function relations in the domain of attention in spina bifida, as well as examining the utility of using alternative statistics to estimate those relations.

Overview of the factors affecting correlation

A considerable number of factors might affect the true value of the correlation between two constructs, while numerous additional factors affect the estimation of that relation and the distributional properties of any particular estimator. The present study focuses on different statistical methods that have been proposed for estimating the relation between two constructs. Interest in these different estimators arises out of their purported insensitivity to / robustness against conditions that might adversely affect the use of traditional, parametric measures of relation, namely, the Pearson Correlation coefficient, ρ , and its associated sample estimator, r . The estimators to be examined in the present study were chosen because various issues that are known to affect the correlation and its estimation potentially arise in the study of structure-function relations in clinical populations, where studies typically employ smallish samples, rely on individual measures to operationalize constructs, and where the population score distributions are not bivariate-normal. Univariate and bivariate distributions of independent and dependent variables (including the problem of outliers), small sample size, apparent group structure to the data, heteroscedasticity, ratio variables, as well as curvilinearity are among the most common factors affecting the magnitude of the population correlation and its estimation (Cohen, Cohen, West, & Aiken, 2003; Hays, 1994). Additional issues may arise when a model contains more than one independent variable. More precisely, misspecification of independent variables included in a model, dependence of residuals, differential reliability of independent variables, and multicollinearity across the independent variables may affect the estimation of coefficients and their standard errors (Cohen et al., 2003). Awareness and understanding of factors affecting estimates are very important in order to select appropriate statistical methods. The following section discusses

potential factors affecting the estimation of correlation in clinical populations using small samples.

Distributional properties of measures. Shape of the distribution, outliers, and error of measurement (also known as an unreliability of measures) are among the most common factors affecting estimates of a correlation. A correlation coefficient has a maximum value equal to one only when two variables have identically shaped distributions. Thus, differences in distribution shapes of dependent and independent variables may affect the magnitude of the correlation. The correlation coefficient is attenuated when distributions of both variables are skewed in opposite directions, and variables reflecting an underlying construct have a limited number of response possibilities (Cohen et al., 2003). This situation commonly occurs with dichotomous, and polytomous variables. Therefore, a scale on which dependent and independent variables are measured potentially affects estimation of correlation. In general, scales with more values are better for capturing individual differences. Consequently, they reduce the risk of attenuating the relationship between independent and dependent variables (Cohen et al., 2003). Summarizing, the magnitude of a correlation might be affected by dissimilarities of distributions of dependent and independent variables, as well as by scales, on which those variables are measured.

Estimation of correlation might also be affected by the presence of outliers. Outliers can be interpreted as data points which deviate substantially from the remaining data in the data set (Cohen et al., 2003). Additionally, their residuals may have high values when one measure is predicted from another. That is to say, an individual data point may be extreme in univariate space, or bivariate space, or both. It is possible for an observation to be extreme in bivariate space, but not in univariate space, such as a person whose score falls at the 10th

percentile for weight and the 90th percentile for height. Such an individual is not unusual with respect to height, or weight, but only in the two-dimensional space of height and weight together. Outliers may result from unusual cases occurring in the data, errors in data collection and/or errors in entering data. Their occurrence may affect estimation of correlation coefficients and their standard errors, and therefore weaken inferences. More specifically, outliers might “dominate” obtained results. In other words, obtained results might be heavily influenced by the presence of one or more outliers (Cohen et al., 2003). It is possible that one outlier is sufficient to create spurious results, especially if a sample size is small. Moreover, the presence of outliers may mask relations (Cohen et al., 2003), making measures appear unrelated when, in fact, they are. Sample size tends to mitigate the ability for a single data point to be highly influential and, in that sense, analyses performed on larger sample sizes are to a certain degree robust to the presence of outliers.

Another factor associated with distributional properties of measures, which may affect estimates of correlation, is related to the reliability of measures. Reliability reflects the degree to which variability in test performance is systematic. In classical test theory, reliability is the proportion of observed score variation that is attributable to true score variation, whereas in modern test theory, reliability is replaced by concepts of test score precision, which is inversely related to the standard error of measurement. For unidimensional measures, reliability is the proportion of score variance that is attributable to the construct being measured by the measure. Random error in scores does not, by definition, relate systematically to variability in other scores. Consequently, it can be shown algebraically that the population correlation between two observed measures is equal to the population correlation between the true scores divided by the square root of the product of

the reliabilities of the measures (Kenny, 1979). Put simply, unreliability in measures attenuates the population correlation between observed scores relative to the population correlation between the true scores. To the extent that our interest is always in estimating the correlation between constructs rather than between the measures that simply operationalize those constructs in a given study, unreliability in measures weakens inferences about relations between constructs. In bivariate correlation, error of measurement results in underestimation of correlation (Cohen et al., 2003). In other words, a population correlation between true scores will be higher compared to an estimated correlation between observed scores. When there are more than two independent variables, the correlation might be overestimated or underestimated due to relations with other variables in the model. Rarely, a measurement error results in correct estimation (Cohen et al., 2003). Summarizing, unreliability results in biased estimation of true-score correlation coefficients and their standard errors, and hence incorrect significance tests and confidence intervals (Cohen et al., 2003).

A problem closely related to the reliability of measures is the restriction of range resulting from the sampling procedure. The restriction of range occurs when some limits on the values of the variables are posed by sampling procedures. In other words, not all values (a full range) of variables are sampled. Therefore, analyses are conducted only on the selected range, where the maximum and/or minimum values might be trimmed. The restriction of range commonly results in the attenuation of correlation. However, it is also possible that a correlation will be overestimated. Overestimated correlation occurs when the proportion of “cases” in a sample deviates substantially from the proportion of “cases” in a population (Cohen et al., 2003). Additionally, the restriction of range may increase correlation in a

situation, where it eliminates curvilinearity. In clinical studies restriction of range might be used in order to eliminate or exclude cases with certain characteristics, e.g., low intelligence, or limited proficiency in the language of testing.

Group structure to the data. Another important consideration is any group structure that might be present in the data resulting from the inclusion of heterogeneous subgroups in the study population. The presence of group structure to the data can significantly distort the correlation between two measures. For example, it can be shown that, in the presence of a multi-group structure, the correlation disregarding group is a function of the pooled-within groups relation between the measures and the between groups relation between the measures. For example, the relationship between measures of attention and measures of arithmetic skill might be affected by the presence or absence of attention deficit / hyperactivity disorder (ADHD) and/or the presence of math disability. If one estimated the correlation in a mixed population consisting of individuals with and without ADHD and with and without math disability, that relation would be a function of the within group relations between attention and arithmetic and the degree to which the groups differ on the measures of attention and the measures of arithmetic. Ignoring the group structure to the data might result in underestimation or overestimation of the correlation. Therefore, it is not recommended to ignore the group structure to the data. Computation of a correlation coefficient without considering the structure to the data (referred as a total-groups analysis) commonly overestimates a correlation, because variability of scores is not attributed to the subgroups. In other words, individual cases are treated as a whole group, in which all cases are similar (have no structure) (Cohen et al., 2003). On the other hand, computation of correlation coefficients for each group separately (referred as within-groups analysis) limits external

validity of the results (Cohen, et al., 2003). The most efficient approach is computation of correlation between the independent variable and the dependent variable while accounting for the group membership (Cohen et al., 2003). More specifically, inclusion of the group membership allows for controlling variability in the means of the groups.

Heteroscedasticity. Homoscedasticity assumes constant variance of residuals for all values of an independent variable (Cohen et al, 2003). Consequently, heteroscedasticity occurs when residual variance is not constant for all values of an independent variable. Heteroscedasticity results in biased estimation of standard errors of coefficients. However, the estimation of coefficients is correct (Cohen et al., 2003). Cohen and colleagues (2003) suggest that a ratio of residual variance at various values of the independent variable which is greater than 10 should be considered heteroscedastic.

Small sample size. Sample size affects power as well as estimation of standard errors, and consequently, confidence intervals and significance tests. The width of the confidence interval decreases with smaller standard errors, which depends on the sample size, all other things being equal (Hays, 1994). Correlation coefficients, which are based on the standard deviations of independent and dependent variables, are more accurate, when sample sizes are bigger. Moreover, sample size influences the distribution of the variables, which in turn potentially affects the accuracy of estimates of correlation coefficients. Additionally, small sample size increases the “effect of outliers”. In other words, bigger sample size reduces the effect of outliers on estimates of correlation coefficients.

Alternative statistics estimating structure-function relations

The above comments regarding sensitivity of the correlation to various distributional properties of measures concern the Pearson correlation coefficient. Different statistical

approaches might be used instead of Pearson's correlation in order to estimate variable relations. Alternative statistical approaches such as robust measures of correlation can assist investigators when confronted with small samples and multivariate non-normal data. Robust correlations provide different conceptualization of population correlation compared to the Pearson's correlation. In particular, the robust correlations estimate the robust population correlations, whereas the Pearson's correlation estimates the Pearson's population correlation. Despite different conceptualization of population correlation, both, the robust correlations and the Pearson's correlation are estimators of the degree of linear relation between two measures. When variables are independent the coefficients of robust correlations and Pearson's correlation are equal to 0. Consequently, when variables are perfectly dependent the coefficients of robust correlations and Pearson's correlation are equal to 1.

Wilcox (2005) divides robust correlation measures into two groups: (a) correlations that are robust to the outliers but do not consider the overall structure of the data (for instance, the percentage bend and winsorized correlations), and (b) correlations that are robust to the outliers and heteroscedasticity, and that consider the overall structure of the data (for instance, the skipped correlations). A detailed description of all robust correlation measures is beyond the scope of the present study. The present study focuses on utilization of selected robust correlation measures which can strengthen inferences about structure-function relations in small clinical samples where data might not be normally distributed, and outliers are present.

The Percentage Bend Correlation. The percentage bend correlation is an alternative method used in estimating a degree to which variables are dependent. The percentage bend

correlation does not estimate the Pearson's population correlation, it estimates the population percentage bend correlation, which is more robust to violations of normality and presence of univariate outliers, but it is not robust to heteroscedasticity. The breakdown point¹ of the percentage bend correlation is equal to β . A commonly used value of β in the percentage bend correlation is 0.2, which means that up to 20% of data (observations) might be contaminated without resulting in biased outcomes (Wilcox, 1994). The percentage bend correlation estimates the population correlation differently than the Pearson's correlation. The percentage bend correlation should not be used when the Pearson's population correlation is intended to be estimated (Wilcox, 1994; Wilcox, 2005). When the variables are normally distributed, the percentage bend correlation gives comparable estimates to the Pearson's correlation. However, the percentage bend correlation is more robust even to the small deviations from the normal distribution and occurrence of outliers (Wilcox, 1994). For the Pearson correlation, power is affected by the distributional properties of the variables. High skewness and heavy-tail distributions significantly decrease the power and increase the type I error probability related to the Pearson's correlation, but they do not affect the power and the type I error probability associated with the percentage bend correlation. The power of the percentage bend correlation and the type I error probability are not affected by high skewness and heavy-tail distribution.

The Winsorized Correlation. The Winsorized Correlation is another alternative estimator of the degree of linear relation between two measures, which might be used when the variables are not normally distributed and outliers are present. The Winsorized correlation is however, sensitive to heteroscedasticity. The population Winsorized correlation

¹ The breakdown point is associated with a global robustness of estimator. In particular, the breakdown point reflects the maximum amount of model misspecification which an estimator can handle before estimation bias is too high (Heritier, Cantoni, Copt, & Victoria-Feser, 2009).

is estimated using Winsorized observations (Wilcox, 2008). More specifically, the Winsorized correlation can be understood as a two-step approach. First, a specific percentage of observations located at the end of the distribution is Winsorized (i.e., replaced) with adjacent observations. In other words, the smallest and the highest observations are replaced with adjacent observations. For instance, with commonly used 20% Winsorization, the fraction of the replaced observations is equal to 10 ($g = .1$), which means that one in 10 observations from each end of the distribution is replaced with that observation that lies adjacent to that observation that lies next closest to that portion of the data that is not being replaced. Concretely, if the observations are ordered from 1 to n and the first and last k observations are to be Winsorized (that is, observations $i = 1$ to k and observations $i = n-k, n$ are to be replaced), then observations 1 to k are replaced with observation $k+1$ *and* observations $n-k$ to n are replaced with observation $n-k-1$. After Winsorizing the observations the correlation is estimated on the Winsorized observations using the Pearson's correlation. Power and type I error probabilities of the Winsorized correlation are less affected by non-normal distribution (high skewness and heavy-tail) when compared with the Pearson's correlation. However, the percentage bend correlation is on average more robust to violations of normality than the Winsorized correlation.

The skipped correlations. Like the Winsorized correlation, which varies depending on the percentage of the data that is replaced, there are multiple approaches to computing a skipped correlation. Hence, this section discusses the skipped correlations as a set, as well as individually. In general, the skipped correlations are more robust to multiple outliers (including multivariate outliers) and violations of normality than the percentage bend and Winsorized correlations. The skipped correlations attempt to correct estimation of variable

relations by accounting for the overall structure of the data, which is associated with notions about observational depth and its measurement. The skipped correlations utilize measures (such as projection methods using Donoho-Gasko Median or Minimum Volume Ellipsoid estimator) that take into consideration how deeply an observation is nested within cloud of data (Wilcox, 2003; Wilcox, 2010). Skipped correlations estimate correlations using a two-step approach. First, measures of depth are used to flag and eliminate outliers, which are interpreted as data points with the lowest measures of depth. Then, the Pearson correlation is estimated on the data from which outliers have been removed. It is noteworthy, that when desired the Spearman's rho correlation can also be estimated on the remaining data instead of the Pearson correlation.

The skipped correlation using Donoho-Gasko Median (DGM). The skipped correlation using DGM is used to estimate correlation on the observations from which outliers were eliminated. The breakdown point of the skipped correlation using DGM is equal to 0.50, which means that up to 50% of the data (observations) might be contaminated without resulting in biased outcomes (Wilcox, 2008). Skipped correlations using DGM use a two-step approach. First, the DGM estimator flags and eliminates outliers. The halfspace depth² is calculated for each observation. The observations with the highest measures of depth (deepest points) are used to estimate the center of the distribution. Observations, which are not nested deeply enough within the overall structure of the data are classified as outliers. Specifically, the Donoho-Gasko median is the average computed on all observations with the largest depth (Wilcox, 2008). Once the outliers are eliminated from the data set the Pearson's correlation is estimated on the remaining data (Wilcox, 2005).

² The halfspace depth is a measure used for estimating how deeply an observation is nested within a cloud of all data points (Wilcox, 2003).

The skipped correlation using Minimum Volume Ellipsoid (MVE). The skipped correlation using MVE estimates the correlation with the data from which outliers were previously removed based on the MVE estimator. The first step in the skipped correlation is detection and removal of the outliers using the minimum volume ellipsoid estimator (MVE; Wilcox, 2008). The MVE method seeks to find the subset of the data with the smallest ellipsoid volume capturing a specific percentage of the total data. In other words, at first all data (observations) are divided into different subsets each containing approximately 50% of the observations. Afterwards, the subset which occupies the smallest volume is selected (van der Linde & Houle, 2006). The smallest ellipsoid holding 50% of the data is used to calculate the measure of location and covariance, which are then used to estimate the distance of all data points from the center of the distribution the measure of location and covariance. The data points, which do not fit within the cut-off points, are classified as outliers. Once the outliers are no longer present in the data the Pearson's correlation is estimated on the remaining data (Wilcox, 2005; Wilcox, 2008).

Purpose of the study

Structure-function relations in the domain of attention are not well understood. Limited research findings may stem from problems in estimating these relations in small samples combined with data distributions that do not conform to the assumptions of the statistics used to estimate the relations. Therefore, the present study focused on estimating structure-function relations in small clinical samples where data might not be normally distributed. More specifically, it investigated factors affecting the study of structure-function relations in the domain of attention in spina bifida and the utility of using alternative statistics to estimate those relations.

Method

Participants

The participants were evaluated in a larger study examining cognitive and neurobiological variability in spina bifida meningomyelocele and related disorders. There were 111 participants (82 spina bifida, 29 normal controls) in the sample used to estimate behavior-behavior relations. The sample used to estimate structure-function relations consisted of 61 participants (43 spina bifida, 18 normal controls). The decreased number of participants available to estimate structure-function relations was due to the lack of magnetic resonance imaging (MRI) data on participants. The reason for missing data differed across the two groups. Specifically, 39 children with spina bifida had MRI scans that could not be used to compute volumetric measures because their brains were too deformed to determine necessary landmarks and reference points, and/or could not be adequately transformed to yield volumetric measures. Additionally, MRI was not obtained for 11 typically developing participants. Socio-demographics, handedness and IQ information about the sample used to estimate behavior-behavior relations as well as the sample used to estimate structure-function relations are presented in table 1.

Table 1.*Sociodemographic and Handedness Information by Etiology Group*

	Behavioral-behavioral relations		Structure-function relations	
Group Type	<i>NC</i>	<i>SBM</i>	<i>NC</i>	<i>SBM</i>
N	29	82	18	43
Gender - n (%)				
Male	14 (48.3%)	50 (61.0%)	9 (50.0%)	26 (60.5%)
Female	15 (51.7%)	32 (39.0%)	9 (50.0%)	17 (39.5%)
Ethnicity - n (%)				
Caucasian	13 (44.8%)	39 (47.6%)	7 (38.9%)	21 (48.9%)
Hispanic	8 (27.6%)	28 (34.1%)	8 (44.4%)	16 (37.2%)
African American	1 (3.5%)	6 (7.3%)	1 (5.6%)	3 (7.0%)
Asian American	5 (17.2%)	6 (7.3%)	1 (5.6%)	3 (7.0%)
Other	4 (6.9%)	3 (3.7%)	1 (5.6%)	0 (0.0%)
Handedness - n (%)				
Left	1 (3.5%)	25 (30.5%)	1 (5.6%)	12 (27.9%)
Right	27 (93.0%)	56 (68.3%)	16 (88.8%)	31 (72.1%)
Ambidextrous	1 (3.5%)	1 (1.2%)	1 (5.6%)	0 (0.0%)
Age (M, SD)	10.0; 2.9	7.6; 3.7	10.1; 3.3	7.7; 4.1
Socioeconomic status (M, SD)	42.8; 12.0	37.3; 12.4	42.8; 12.1	36.5; 12.8
Stanford-Binet composite IQ (M, SD)	107.2; 12.2	87.1; 14.9	107.7; 12.4	90.7; 13.2

In terms of ADHD symptoms, spina bifida and typically developing children had less impulsive-hyperactive symptoms compared to inattentive symptoms.

Materials and Procedures

The Attention Network Test (ANT). The Attention Network Test measures efficiency of three attentional networks: orienting, alerting, and executive control (Posner et al., 2006; Rueda et al., 2004). The attention networks were measured using four types of cues and three types of flankers. The possible cues were: no cue (only the fixation cross), a central cue (an asterisk in the place of the fixation cross), a double cue (asterisks above and below the

fixation cross), or a spatial cue (an asterisk in the place of an upcoming target; Rueda et al., 2004). The target was presented as a drawing of a single yellow fish or a row of five yellow fish appearing above or below the fixation point. Response of a participant was indicated by the direction, in which the central fish pointed. On congruent trials the central fish and flanking fish were facing the same direction; on incongruent trials flanking fish were in the opposite direction from the central fish, whereas on neutral trials the central fish appeared without flanking fish (Rueda et al., 2004). Executive control was assessed using an incongruent flanker, which enforced a participant to resolve a conflict resulting from an opposite direction of a central fish and flanking fish. All types of cues were used in measuring executive control (Johnson et al., 2008). Executive control was measured by deducting reaction times for congruent from incongruent trials. Alerting was assessed by using a cue, which did not carry any spatial information, but carried a warning signal (Rueda et al., 2004). Only neutral and congruent conditions were used in measuring alertness (Johnson et al., 2008). Alerting was measured by deducting reaction times for double cue from no cue trials. Orienting was assessed by using a spatially informative cue as indicator of location of an upcoming target. Only neutral and congruent conditions were used in measuring orienting (Johnson et al., 2008). Orienting was measured by deducting reaction times for spatial cue from central cue trails (Posner et al., 2006).

Test of Everyday Attention for Children (TEA-Ch). The Test of Everyday Attention for Children (Manly, Robertson, Anderson, & Nimmo-Smith, 1999) consisting of nine subtests is utilized in the assessment of different attentional components including selective, sustained, and divided attention (for auditory and visual modalities), switching attention between tasks and attentional control, as well as verbal and motor response inhibition. In the

present study we focused only on the evaluation of attentional control (Opposite Worlds subtest) and sustained attention (Code Transmission).

In the Opposite World subtest children were asked to (a) read a sequenced list of numbers, which was presented to them on the card (same world condition/control) or (b) provide a response by using an alternate number to the presented one on the card, in other words verbal response “one” when seeing digit “2” or verbal response “two” when seeing digit “1” (opposite world condition/ attentional control) (Baron, 2001). Therefore, in the opposite world condition children had to inhibit an initial response in order to respond correctly. The Opposite World subtest was a timed task, in which time was measured for both conditions (each card). The total time for the Opposite World condition was an indicator of the attentional control ability depending on the response inhibition. Incorrect responses resulted in a time penalty, because children could not proceed with the task until they corrected their response.

In the Code Transmission subtest children were asked to listen to an audiotaped recording presenting single digit numbers within 2 second intervals (Baron, 2001). The goal of the task was to say out loud the number, which occurred right before all double 5-digit sequences. In other words, the number occurring right before each 5-5 (Baron, 2001) was to be recalled after hearing the sequence 5-5. Forty target presentations appeared over 12 minutes (Manly et al., 2001). The number of correct responses out of 40 target presentations indicated the total score on the subtest.

The Swanson Nolan Achenbach Pelham-IV Parent Rating Scale (SNAP-IV). The Swanson Nolan Achenbach Pelham-IV Parent Rating Scale (Swanson, 1992) consisting of 90 items is utilized in identifying ADHD and other comorbid conditions diagnosed for the first

time in childhood (Burmeister et al., 2005). This parent and teacher rating scale concentrates on identifying inattention, impulsivity, hyperactivity, and oppositional behaviors. The scale is consistent with ADHD and oppositional defiant disorder (ODD) DSM-IV (American Psychiatric Association, 1994) criteria, items from the Conners Index Questionnaire (Conners, 1984), IOWA Conners Questionnaire (Loney & Milich, 1982), and items from the DSM-IV disorders that may overlap with criteria for ADHD (Burmeister et al., 2005). Parents/teachers rate children on the 4-point scale, where 0 = Not at all, 1 = Just a little, 2 = Quite a bit, 3 = Very much. The total score for each subscale was calculated by adding the number associated with the provided answers for all items within the subscale and dividing that sum by the number of all items in that subscale (Burmeister et al., 2005). Higher scores indicated occurrence of more symptoms. It is worth mentioning that in the present study only items assessing ADHD were used.

Procedures

Attention Network Test procedure. A session of ANT included 24 practice trials and two blocks of 48 experimental trials. Each trial reflected one of 12 possible conditions: three flanker types (congruent, incongruent, and neutral) x four cues (no cue, central cue, double cue, spatial cue; Rueda et al., 2004). All conditions were presented in equal proportion. At the beginning of each trial the fixation cross was presented for 400 – 1600 ms. Afterwards, one of four possible cues was presented for 150 ms. The cue presentation was followed by lasting 450 ms fixation period. After that, the target with flanker or target alone was presented until a response was detected (no longer than 1700 ms). The subject's response was followed by automated feedback indicating a correct or incorrect response. For more details readers are referred to Rueda et al. (2004).

Behavioral assessment procedure. All participants were administered two subtests from the Test of Everyday Attention for Children (TEA-Ch): the Opposite Worlds and the Code Transmission subset. Additionally, parents and teachers completed SNAP-IV for school-aged participants.

MRI scan procedure. Volumetric measures of brain structures were obtained using comparable General Electric Signa 1.5 tesla magnets located in Houston and Toronto. Three imaging sequences were obtained. The initial sequence was in a sagittal plane spin-echo T1-weighted localizer, FOV 24 cm, TR 500ms, TE 14ms, 256×192 matrix, 3 mm with a 0.3 skip, 2 repetitions. Afterwards, two whole brain T1 and T2 coronal acquisitions were obtained in order to ensure accuracy of CSF estimate relatively to the white and grey matter estimates (3D-spoiled gradient-echo with contiguous 1.7 mm coronal images, FOV 24 cm, TR 18ms, TE 3ms, Flip angle 25 degrees, 124 locations, 256×256 matrix, 1 repetition; 3D fast spin-echo T2-weighted sequence, FOV 24 cm, TR 4000ms, TE 102ms, ETL 16, 256×256 matrix, 1 repetition with contiguous 1.7 mm coronal images, respectively). FreeSurfer software was used to obtain volumetric measures of the brain.

Data Analysis

Behavior-behavior relations, as well as structure-function relations were estimated using Test of Everyday Attention for Children, the Attention Network Test, and structural MRI measures. Measures derived from MRI included: the superior parietal cortex, right inferior parietal lobe, dorsolateral prefrontal cortex, anterior cingulate gyrus, and thalamus. Log transformations were applied to reaction time measures.

Descriptive statistics. Distributional properties of variables were visually explored using histograms and boxplots, as well as by computing standard descriptive statistics. Scatterplot

matrices were used to examine potential variable relations. Measures of location and spread, as well as univariate and bivariate skewness and kurtosis were computed for each variable. Furthermore, the modification of Cook-Weisberg statistic derived by Koenker (Wilcox, 2008) was computed in order to detect heteroscedasticity.

Bootstrap. Using alternative estimators of a parameter on a single sample with unknown characteristics limits the inferences that one can draw about the estimators and the relations because it is impossible to discern what one might expect in the long run from applying such a process repeatedly under similar conditions in the future. Similarly, it is impossible to know if similarities and differences between estimators reflect chance characteristics of the current sample, or attributes of the population, including, but not limited to the relation/parameter value in the population. Simply using standard errors estimated from the single sample is of little help. Specifically, statistical inference using a single sample is typically based on computing estimates from that sample and making inferences about characteristics of unobserved populations based on those estimates and their estimated standard errors. Accuracy of estimation, especially the standard errors of estimates and the associated probability statements, depend on certain statistical assumptions and the validity of those assumptions. All of these problems and limitations of comparing estimators using a single sample of field data derived from a population with unknown characteristics can be solved by using a procedure known as the bootstrap (Effron & Tibshirani, 1993).

The bootstrap is a data-based simulation used to support statistical inference by empirically deriving the sampling distributions of statistics from a single sample. The bootstrap is a method which improves accuracy of statistical inferences without relying only on statistical assumptions. In other words, the bootstrap minimizes the required set of

assumptions by empirically deriving an empirical distribution for an estimate. The bootstrap method is a process of random sampling, with replacement, observations from a finite population a large number of times (Efron & Tibshirani, 1993). A single bootstrap sample is obtained by randomly sampling with replacement n times from the original n data points. The sample statistic(s) is(are) computed on this bootstrap sample, and then the entire process is repeated a large number of times to obtain the bootstrap sampling distribution. In the present study we sampled n observations ($n = 111$ or $n = 61$ for the behavior-behavior and structure-function relations, respectively) with replacement a total of 10000 times, computing all five correlations on a given pair of variables on each of the 10,000 bootstrap samples. Separate bootstrap samples were derived for each pair of variables for which the correlation was to be estimated. Empirical distributions of five correlation estimates: the Pearson's correlation, percentage bend correlation, Winsorized correlation, skipped correlation using DGM, and skipped correlation using MVE, were obtained. Distributions of the five correlation estimates for a given relation were derived from the same sample. Summary statistics of distributions, including the mean, standard deviation, and confidence intervals, were computed for each correlation's estimate. By using the bootstrap to simulate the sampling distributions of the five estimators for each of the relations to be studied from this single field sample, it was possible to determine the extent to which variability in estimates differed across estimators, across the relations to be estimated, or both. Furthermore, it was possible to examine the extent to which different estimators were correlated and yielded similar or discrepant estimates in a given sample. Finally, the use of the bootstrap allowed examination of the extent to which these similarities and differences depended on

characteristics of the univariate and bivariate distributions of the variables under investigation.

Comparison of estimates. We used the Pearson's Correlation and four robust correlations: the Percentage Bend Correlation, the Winsorized Correlation, the Skipped Correlation using DGM, and the Skipped Correlation using MVE to examine behavior-behavior relations, as well as, structure-function relations in the domain of attention. A bootstrap sampling process was used to compare performance of the five estimators in this field context. Performance of the five estimators was compared with regards to summary statistics (mean, standard deviation, confidence intervals) of derived distributions, and to examine characteristics of the univariate and bivariate distributions that related to differences across the five estimators.

Results

The results are divided into three sections: descriptive analyses, single sample estimates of population correlation, and bootstrapped estimates of population correlation. Each section describes results with regards to the total groups, spina bifida group and normal controls. To begin, the descriptive analyses section discusses distributional properties of variables as well as verifies the homoscedasticity assumption. In the following section, five single sample estimates of population correlation: the Pearson's correlation, percentage bend correlation, Winsorized correlation, skipped correlation using DGM, and skipped correlation using MVE are compared with respect to their magnitude. More specifically, similarities and differences among the five single-sample estimates are examined in order to improve understanding of behavior-behavior and structure-function relations in the domain of attention. These estimates are equivalent to computing each estimate in the sample of subjects as would

typically be done in a common data analytic situation. Additionally, statistical significance of behavior-behavior and structure-function relations is examined based on the standard error for each statistic. In the last section, bootstrapped estimates of the population correlation are discussed in order to more accurately investigate the inferences that one can draw about the estimators and the relations. Performance of the five estimators is compared with regards to summary statistics (including the mean, standard deviation, and confidence intervals) of their distributions. Finally, characteristics of the univariate and bivariate distributions of the original variables are examined as possible variables to explain the differences observed across the five estimators.

Descriptive Analyses

Variables of interest were explored in order to detect possible violations of statistical assumptions. Most of the behavioral measures (except the attentional control variable) used in the estimation of behavior-behavior and structure-function relations had a leptokurtic distribution in the total and spina bifida groups. At the same time, kurtosis of brain measures was within the normal range in the total and spina bifida groups. In the normal controls, leptokurtic distributions were found for many of the behavioral and brain measures. In terms of skewness, most of the variables in the total groups and within groups were symmetrically distributed. Further details regarding standard descriptive statistics are presented in Table 2. The homoscedasticity assumption was examined using a modification of the Cook-Weisberg statistic derived by Koenker (Table 3). For most pairs of variables variance of the residual errors across different values of X (where X represents an independent variable) was constant. Heteroscedasticity was observed for orienting-alerting and alerting-conflict relations in the total groups and spina bifida group. Additionally, the homoscedasticity assumption was violated in normal controls for the following pairs of variables: alerting-

sustained attention and alerting-attentional control. Visual exploration of boxplots followed by the examination of extreme observations revealed the presence of outliers. With regards to the behavioral measures, alerting and sustained attention were the variables with the most outliers in both the spina bifida group and normal controls. With regards to the brain measures, the dorsolateral prefrontal cortex had the most outliers in spina bifida group, whereas the superior parietal cortex had the most outliers in normal controls. Figures 1a – 1b and 2a – 2b provide examples of outliers in the behavioral and brain measures. Overall, descriptive and exploratory analyses revealed more problems with regards to distributional properties of behavioral measures compared to brain measures.

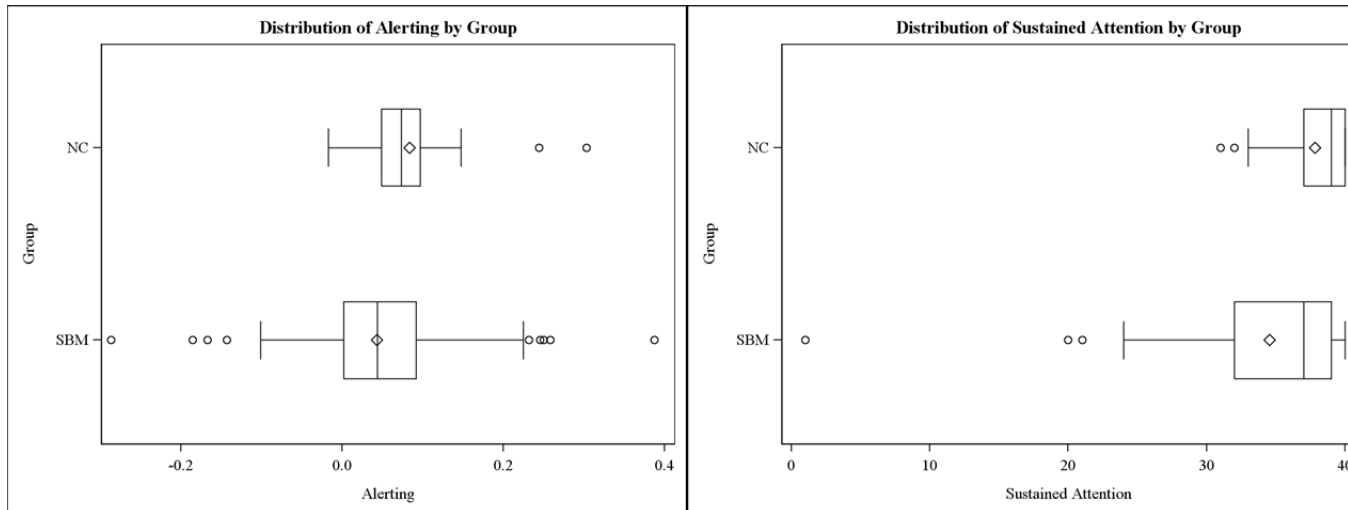


Fig 1a – 1b. Boxplots demonstrating outliers in the selected behavioral measures. Multiple outliers are present in alerting in the spina bifida group and normal controls. Outliers and ceiling effect are present in the sustained attention in the spina

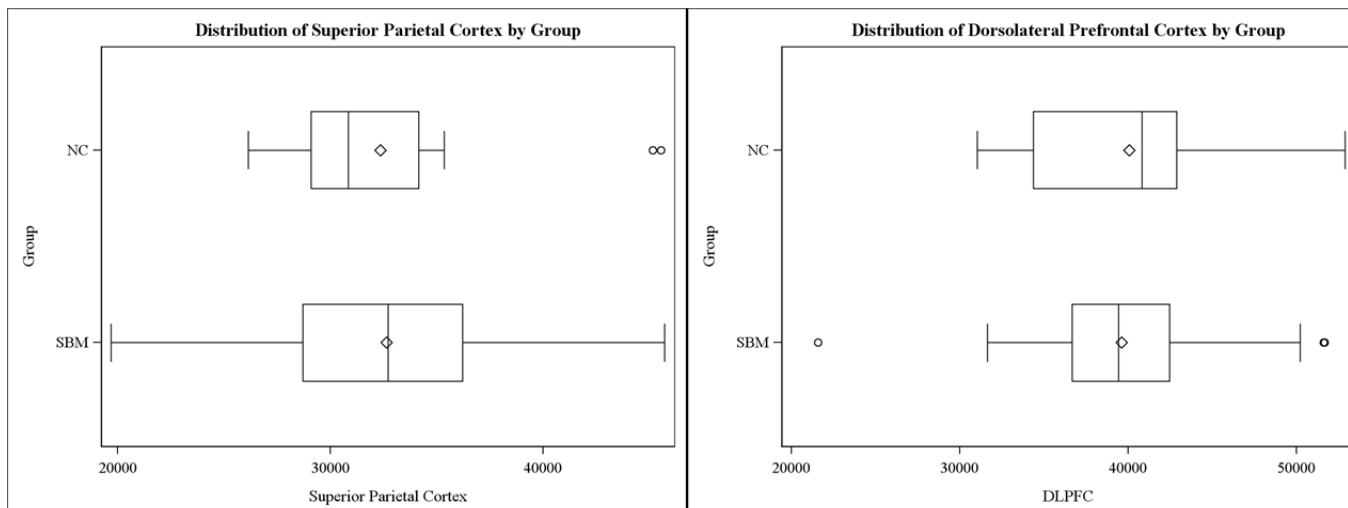


Fig 2a – 2b. Boxplots demonstrating outliers in the selected brain measures. Outliers are present in the superior partial cortex in the normal controls. Outliers are present in the dorsolateral prefrontal cortex in the spina bifida group.

Table 2
Standard Descriptive Statistics for Behavior-Behavior and Structure-Function Relations

BEHAVIOR-BEHAVIOR RELATIONS												
Variable	Total Samples (N = 111)				Spina Bifida Group (N = 82)				Normal Controls (N = 29)			
	Mean	SD	Skewness	Kurtosis	Mean	SD	Skewness	Kurtosis	Mean	SD	Skewness	Kurtosis
Alerting	0.05	0.10	0.06	2.54	0.04	0.10	0.10	2.10	0.08	0.07	1.80	4.47
Orienting	0.06	0.10	1.59	8.96	0.06	0.11	1.79	9.16	0.08	0.07	-0.03	-0.51
Conflict Resolution	0.16	0.12	0.87	2.45	0.16	0.13	0.78	2.07	0.14	0.09	0.92	1.15
Sustained Attention	35.40	5.71	-2.63	11.30	34.54	6.26	-1.36	8.16	37.83	2.55	-1.43	1.21
Attentional Control	3.56	0.34	0.54	0.38	3.64	0.32	0.60	0.43	3.33	0.27	0.63	0.97
STRUCTURE-FUNCTION RELATIONS												
Variable	Total Samples (N = 61)				Spina Bifida Group (N = 43)				Normal Controls (N = 18)			
	Mean	SD	Skewness	Kurtosis	Mean	SD	Skewness	Kurtosis	Mean	SD	Skewness	Kurtosis
Alerting	0.07	0.09	0.78	2.30	0.07	0.10	0.75	2.28	0.09	0.08	1.60	2.94
Orienting	0.07	0.10	2.64	13.81	0.06	0.11	3.11	15.46	0.08	0.08	-0.24	-0.45
Conflict Resolution	0.17	0.14	0.96	1.96	0.17	0.15	0.88	1.67	0.15	0.10	0.89	0.24
Sustained Attention	34.98	6.76	-2.52	9.59	33.86	7.55	-2.22	7.34	37.67	3.11	-1.23	-0.09
Attentional Control	3.51	0.28	0.40	0.20	3.56	0.26	0.33	0.47	3.38	0.28	0.97	1.52
Right Inferior Parietal Lobe	16793.69	3123.42	0.51	-0.09	15817.14	2642.20	0.46	-0.55	19126.56	3001.64	0.36	0.31
Superior Parietal Cortex	32551.33	5553.18	0.43	0.30	32632.37	5671.97	0.06	-0.02	32357.72	5413.07	1.59	2.29
Thalamus	15531.87	2341.05	0.03	-0.90	15195.81	2396.70	0.22	-0.72	16334.67	2045.34	-0.28	-1.23
Dorsolateral Prefrontal Cortex	39748.62	5950.85	-0.01	0.74	39621.88	5740.78	-0.29	1.53	40051.39	6589.84	0.43	-0.36
Anterior Cingulate Cortex	10212.59	2399.55	0.58	-0.13	10230.14	2482.65	0.41	-0.33	10170.67	2256.45	1.24	1.08

Table 3
Homoscedasticity Test for Behavior-Behavior and Structure-Function Relations

Pair of Variables	Homoscedasticity Test for Total Groups	Homoscedasticity Test for Spina Bifida Group	Homoscedasticity Test for Normal Controls
Alerting-Sustained Attention	1.642	2.107	8.402**
Alerting-Conflict Resolution	7.793**	7.211**	0.327
Alerting-Attentional Control	0.708	0.236	11.318***
Alerting-Orienting	9.700**	10.732**	0.674
Sustained Attention-Attentional Control	2.090	0.717	0.049
Conflict Resolution-Sustained Attention	1.024	1.096	0.081
Conflict Resolution-Attentional Control	0.003	0.121	0.095
Orienting-Sustained Attention	0.673	0.366	0.056
Orienting-Conflict Resolution	0.586	0.522	0.004
Orienting-Attentional Control	1.062	0.770	0.102
Alerting-Right Inferior Parietal Lobe	0.158	0.033	1.058
Alerting-Thalamus	0.649	1.350	0.030
Sustained Attention-Anterior Cingulate Cortex	0.051	0.087	0.905
Sustained Attention-Dorsolateral Prefrontal Cortex	0.940	1.203	0.744
Conflict Resolution-Anterior Cingulate Cortex	0.508	1.232	0.587
Conflict Resolution-Dorsolateral Prefrontal Cortex	1.168	0.738	0.484
Attentional Control-Anterior Cingulate Cortex	1.126	0.738	0.784
Attentional Control-Dorsolateral Prefrontal Cortex	0.103	0.155	0.011
Orienting-Superior Parietal Cortex	0.393	0.593	0.028
Orienting-Thalamus	2.123	2.193	0.271

Note. *** $p < .001$. ** $p < .01$. * $p < .05$.

Single Sample Estimates of Population Correlation

Total Groups. Table 4 shows five single sample estimates of the population correlations for the behavior-behavior and structure-function relations in the total groups. Two distinct patterns of relations were observed: (1) all estimators performed similarly, (2) the estimate of the skipped correlation using MVE differed from the other three robust estimators, which were comparable to the Pearson estimate. With regards to the first pattern of results, the magnitude of the correlation coefficients was comparable for all five estimators irrespective of the type of investigated relation (the behavior-behavior vs. structure-function relation). In the second pattern of findings, the magnitude of the skipped correlation using MVE was higher or lower when compared with the magnitude of the other three robust estimators, which were comparable to the Pearson estimate. Because of insufficient variability of certain variables, computation of the skipped correlation using MVE was not always possible.

In order to assess the statistical significance of the examined relations, significance tests were compared across all estimators. More specifically, statistical significance of a given relation was assumed only for correlations where all estimators were statistically significant, which warranted reliable results. Consequently, statistically significant correlation across all estimators was only found for sustained attention and attentional control (more details in Table 4). More specifically, there was a negative relation between sustained attention and attentional control as measured by reaction time, which meant that children with shorter reaction times signifying higher attentional control had more correct responses suggesting better sustained attention capacity. In addition, the function in *R* used to compute the skipped correlations using MVE did not provide a significance test, because no simple test of the hypothesis of zero correlation has yet been for the MVE method (Wilcox, 2008).

Table 4*Single Sample Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Total Groups)*

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
Alerting-Sustained Attention	-0.017	0.036	0.013	0.078	-0.018
Alerting-Conflict Resolution	0.051	0.029	-0.009	0.056	0.091
Alerting-Attentional Control	0.044	-0.007	-0.004	-0.135	-0.079
Alerting-Orienting	0.275**	0.093	0.077	0.073	0.087
<u>Sustained Attention-Attentional Control</u>	<u>-0.454***</u>	<u>-0.517***</u>	<u>-0.510***</u>	<u>-0.428*</u>	<u>-0.241</u>
Conflict Resolution-Sustained Attention	0.075	0.004	-0.004	0.022	-0.081
Conflict Resolution-Attentional Control	-0.009	-0.021	-0.006	0.009	-0.035
Orienting-Sustained Attention	0.171	0.190*	0.174	0.108	-0.247
Orienting-Conflict Resolution	-0.188*	-0.032	-0.018	0.048	0.193
<i>Orienting-Attentional Control</i>	<i>-0.039</i>	<i>-0.017</i>	<i>-0.032</i>	<i>0.051</i>	<i>-0.037</i>
Alerting-Right Inferior Parietal Lobe	0.112	0.159	0.154	0.150	0.177
<u>Alerting-Thalamus</u>	<u>0.025</u>	<u>-0.088</u>	<u>-0.119</u>	<u>0.025</u>	<u>-0.210</u>
Sustained Attention-Anterior Cingulate Cortex	0.036	-0.031	-0.088	0.036	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	-0.162	0.001	-0.043	-0.162	0.447
<i>Conflict Resolution-Anterior Cingulate Cortex</i>	<i>-0.255*</i>	<i>-0.279*</i>	<i>-0.263*</i>	<i>-0.255</i>	<i>-0.298</i>
Conflict Resolution-Dorsolateral Prefrontal Cortex	-0.210	-0.194	-0.151	-0.083	-0.210
Attentional Control-Anterior Cingulate Cortex	-0.063	-0.010	0.074	-0.008	NA
Attentional Control-Dorsolateral Prefrontal Cortex	-0.028	-0.003	0.064	-0.039	0.141
Orienting-Superior Parietal Cortex	0.006	0.002	-0.006	-0.067	-0.073
Orienting-Thalamus	0.270*	0.316*	0.353**	0.270	0.339

Note. Behavior-Behavior Relations N = 111; Structure-Function Relations N = 61

*** p < .001. ** p < .01. * p < .05.

NA - Insufficient variability in order to use the estimator

Italic - Estimators perform similarly

Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate

Spina Bifida Group. Single sample estimates for the behavior-behavior and structure-function relations in the spina bifida group are presented in Appendix A. In general, three patterns of relations were found: (1) all estimators performed similarly, (2) the Pearson estimate was higher compared to the four robust estimators (the pattern was only found in the behavior-behavior relations), (3) the estimate of skipped correlation using MVE was higher or lower when compared with the other three robust estimators, which were comparable to the Pearson estimate. Because of insufficient variability of certain measures computation of the skipped correlation using MVE was not always possible. Similarly to total groups, statistically significant correlation across all estimators was only found for sustained attention and attentional control (see Appendix A). As previously stated, there is no available test of significance for correlation based on MVE in a single sample (Wilcox, 2008).

Normal Controls. Single sample estimates for behavior-behavior and structure-function relations for the control group are presented in Appendix B. Overall, the magnitude of correlation coefficients across the five estimates was not comparable. The only apparent pattern of relations indicated that the skipped correlation using MVE differed from the other three robust estimators, which were comparable to the Pearson estimate. The magnitude of the skipped correlation using MVE was higher or lower compared to other robust coefficients, which were similar to the Pearson's estimate. Computation of the skipped correlation using MVE was not always possible because of limited variability in one or more measures involved in a relation. No statistically significant correlations were found across all estimators that allow for significance testing in a single sample (see Appendix B).

Bootstrapped Estimates of Population Correlation

The single sample estimates show what would have happened if the different estimates had all been computed on a single study sample. It is difficult to discern whether any patterns observed from such an analysis reflect general properties of the estimators or idiosyncratic characteristics of the particular sample and relation under study. A common approach to solving this problem is to employ simulation techniques so that one can control the true state of the world. An alternative is to use the bootstrap to repeatedly resample with replacement from the original sample, thereby allowing a single sample of data to inform about how each estimator performs more generally, albeit still under unknown conditions. A total of 10,000 bootstrap samples were generated for each relation and all five estimates were computed for each bootstrap sample. Results from the 10,000 samples were used to determine the expected value for each estimator for each relation as well as the empirical standard error of the estimate and shape of the sampling distribution.

Total Groups. The mean values of each of the estimates across the 10,000 bootstrap samples for each relation are presented in Table 5. Based on these mean values two patterns of relations between estimators were found. First, it was clear that for many relations, all five estimators yielded comparable values. More specifically, the means of the bootstrapped estimates were similar across the behavior-behavior and structure-function relations for all five estimators. The second frequently occurring pattern resulted in the mean value for the MVE being different from the other robust estimators, all of which were comparable to Pearson correlation.

In contrast to the multiple patterns that were observed for the means of the different estimators, the standard deviations of the bootstrapped estimates showed one distinct pattern

across the behavior-behavior and structure-function relations (Table 6). In particular, the standard deviations of the sampling distributions for the MVE based estimates were always larger than the empirical standard deviations of the other three robust correlations, which were similar to the standard deviations for the Pearson correlations. This pattern was more pronounced for the structure-function relations than for the behavior-behavior relations. Consequently, confidence intervals based on percentiles of the bootstrap distributions (Table 7) were wider for the skipped correlation using MVE than the other three robust correlations, which were comparable to confidence intervals for the Pearson correlation. Because of insufficient variability for some measures, computation of summary statistics of bootstrap replicates was not always possible. In general, the patterns found for the bootstrapped estimates were consistent with the patterns observed for the single sample estimates.

Table 5*Mean Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Total Groups)*

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
Alerting-Sustained Attention	-0.004	0.030	0.019	0.049	0.029
Alerting-Conflict Resolution	0.051	0.027	-0.006	0.047	0.032
Alerting-Attentional Control	0.044	-0.004	-0.010	-0.093	-0.027
Alerting-Orienting	0.253	0.094	0.075	0.059	0.025
<u>Sustained Attention-Attentional Control</u>	<u>-0.460</u>	<u>-0.515</u>	<u>-0.504</u>	<u>-0.468</u>	<u>-0.269</u>
Conflict Resolution-Sustained Attention	0.066	0.002	-0.010	0.043	-0.070
Conflict Resolution-Attentional Control	-0.008	-0.018	-0.008	-0.030	-0.039
<i>Orienting-Sustained Attention</i>	<i>0.179</i>	<i>0.179</i>	<i>0.166</i>	<i>0.117</i>	<i>-0.111</i>
Orienting-Conflict Resolution	-0.178	-0.034	-0.015	0.026	0.123
Orienting-Attentional Control	-0.042	-0.018	-0.029	0.010	-0.044
Alerting-Right Inferior Parietal Lobe	0.116	0.158	0.154	0.137	0.194
Alerting-Thalamus	0.019	-0.077	-0.119	0.019	-0.280
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	-0.138	-0.017	-0.039	-0.136	0.242
Conflict Resolution-Anterior Cingulate Cortex	-0.257	-0.279	-0.255	-0.259	-0.212
Conflict Resolution-Dorsolateral Prefrontal Cortex	-0.203	-0.182	-0.154	-0.138	-0.074
<u>Attentional Control-Anterior Cingulate Cortex</u>	<u>-0.064</u>	<u>0.001</u>	<u>0.061</u>	<u>-0.024</u>	<u>0.420</u>
Attentional Control-Dorsolateral Prefrontal Cortex	-0.026	0.003	0.057	-0.028	0.145
<i>Orienting-Superior Parietal Cortex</i>	<i>0.010</i>	<i>-0.003</i>	<i>-0.014</i>	<i>-0.028</i>	<i>0.001</i>
Orienting-Thalamus	0.269	0.311	0.346	0.273	0.455

Note. Behavioral Relations N = 111; Structure-Function Relations N = 61

NA - Insufficient variability or sample size is too small in order to use estimators

Italic - Estimators perform similarly (the first pattern)

Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate (the second pattern)

Table 6

*Standard Deviations of Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations
(Total Groups)*

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
Alerting-Sustained Attention	0.126	0.102	0.099	0.121	0.183
Alerting-Conflict Resolution	0.125	0.098	0.097	0.113	0.149
Alerting-Attentional Control	0.105	0.106	0.103	0.147	0.150
Alerting-Orienting	0.161	0.101	0.099	0.119	0.172
Sustained Attention-Attentional Control	0.066	0.068	0.075	0.077	0.176
Conflict Resolution-Sustained Attention	0.087	0.095	0.095	0.095	0.156
Conflict Resolution-Attentional Control	0.084	0.097	0.095	0.120	0.174
<u>Orienting-Sustained Attention</u>	<u>0.084</u>	<u>0.093</u>	<u>0.096</u>	<u>0.100</u>	<u>0.204</u>
Orienting-Conflict Resolution	0.106	0.101	0.098	0.118	0.190
Orienting-Attentional Control	0.103	0.098	0.098	0.120	0.167
Alerting-Right Inferior Parietal Lobe	0.112	0.125	0.132	0.117	0.224
Alerting-Thalamus	0.126	0.132	0.137	0.127	0.238
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA
<u>Sustained Attention-Dorsolateral Prefrontal Cortex</u>	<u>0.159</u>	<u>0.141</u>	<u>0.150</u>	<u>0.164</u>	<u>0.339</u>
Conflict Resolution-Anterior Cingulate Cortex	0.085	0.118	0.131	0.087	0.298
Conflict Resolution-Dorsolateral Prefrontal Cortex	0.150	0.134	0.137	0.152	0.354
Attentional Control-Anterior Cingulate Cortex	0.153	0.150	0.146	0.173	0.287
Attentional Control-Dorsolateral Prefrontal Cortex	0.129	0.134	0.134	0.137	0.262
Orienting-Superior Parietal Cortex	0.099	0.127	0.133	0.107	0.270
Orienting-Thalamus	0.114	0.118	0.119	0.115	0.218

Note. Behavioral Relations N = 111; Structure-Function Relations N = 61

NA - Insufficient variability or sample size is too small in order to use estimators

Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate

Table 7*Confidence Interval of Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Total Groups)*

Pair of Variables	Pearson Correlation		Percentage Bend Correlation		Winsorized Correlation		Skipped Correlation using Donoho-Gasko Median		Skipped Correlation using MVE	
	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)
Alerting-Orienting	-0.029	0.502	-0.074	0.259	-0.089	0.237	-0.140	0.242	-0.265	0.293
Alerting-Conflict Resolution	-0.155	0.256	-0.135	0.188	-0.167	0.152	-0.142	0.228	-0.227	0.260
Alerting-Sustained Attention	-0.202	0.210	-0.138	0.197	-0.143	0.181	-0.159	0.239	-0.285	0.322
Alerting-Attentional Control	-0.131	0.215	-0.175	0.171	-0.179	0.158	-0.313	0.170	-0.257	0.241
Orienting-Conflict Resolution	-0.342	0.009	-0.202	0.131	-0.172	0.147	-0.168	0.220	-0.202	0.421
<u>Orienting-Sustained Attention</u>	<u>0.051</u>	<u>0.323</u>	<u>0.024</u>	<u>0.329</u>	<u>0.005</u>	<u>0.321</u>	<u>-0.048</u>	<u>0.275</u>	<u>-0.425</u>	<u>0.236</u>
Orienting-Attentional Control	-0.218	0.121	-0.178	0.142	-0.189	0.133	-0.195	0.199	-0.344	0.220
Conflict Resolution-Sustained Attention	-0.088	0.197	-0.155	0.159	-0.167	0.148	-0.118	0.195	-0.332	0.187
Conflict Resolution-Attentional Control	-0.144	0.132	-0.178	0.140	-0.165	0.148	-0.227	0.166	-0.313	0.253
Sustained Attention-Attentional Control	-0.571	-0.353	-0.619	-0.398	-0.620	-0.374	-0.589	-0.340	-0.557	0.020
<u>Orienting-Superior Parietal Cortex</u>	<u>-0.145</u>	<u>0.178</u>	<u>-0.211</u>	<u>0.206</u>	<u>-0.236</u>	<u>0.201</u>	<u>-0.201</u>	<u>0.149</u>	<u>-0.434</u>	<u>0.462</u>
Orienting-Thalamus	0.068	0.439	0.111	0.499	0.143	0.536	0.069	0.445	0.105	0.771
Alerting-Thalamus	-0.195	0.225	-0.295	0.139	-0.343	0.110	-0.198	0.226	-0.673	0.104
Alerting-Right Inferior Parietal Lobe	-0.069	0.301	-0.051	0.363	-0.068	0.372	-0.056	0.330	-0.170	0.558
Conflict Resolution-Dorsolateral Prefrontal Cortex	-0.444	0.050	-0.397	0.047	-0.375	0.078	-0.404	0.099	-0.578	0.549
Conflict Resolution-Anterior Cingulate Cortex	-0.394	-0.113	-0.463	-0.080	-0.460	-0.033	-0.401	-0.111	-0.622	0.376
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	-0.388	0.132	-0.254	0.213	-0.290	0.210	-0.396	0.143	-0.551	0.648
Attentional Control-Anterior Cingulate Cortex	-0.307	0.199	-0.245	0.249	-0.182	0.299	-0.296	0.278	-0.126	0.782
Attentional Control-Dorsolateral Prefrontal Cortex	-0.237	0.190	-0.215	0.228	-0.162	0.281	-0.249	0.203	-0.322	0.532

Note. Behavioral Relations N = 111; Structure-Function Relations N = 61

NA - Insufficient variability or sample size is too small in order to use estimators

Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate

All five estimates were computed for each of the 10,000 bootstrap samples. Consequently, it was possible to compare values for different estimators from the same sample and to examine the degree to which similar values resulted from each of the different estimation methods in any given sample. Examination of these joint distributions showed that for any given behavior-behavior relation, were the Pearson correlation, the percentage bend correlation, and the Winsorized correlation were all highly related. Additionally, the Winsorized correlation tended to correlate highly with the percentage bend and the skipped correlation using Donoho-Gasko median. Lastly, the percentage bend correlation was strongly related to the skipped correlation using Donoho-Gasko median. At the same time, the skipped correlation using MVE did not seem to be highly correlated to the other robust estimators nor to the Pearson correlation. Figure 3 demonstrates relations among the five estimators for a specific pair of behavioral measures.

A similar pattern occurred for the structure-function relations, revealing high correlations between the Pearson, percentage bend, Winsorized, and skipped correlation using Donoho-Gasko median. Additionally, the Winsorized correlation was highly correlated with the percentage bend and skipped correlation using Donoho-Gasko median. Lastly, the percentage bend correlation was strongly related to the skipped correlation using Donoho-Gasko median. At the same time, the skipped correlation using MVE did not seem to be highly correlated with the other robust estimators nor with the Pearson correlation. Figure 4 demonstrates relations across the five estimators for a specific pair of behavioral and brain measures. Similar patterns were observed for the other structure-function relations, which are not depicted graphically in the interest of space.

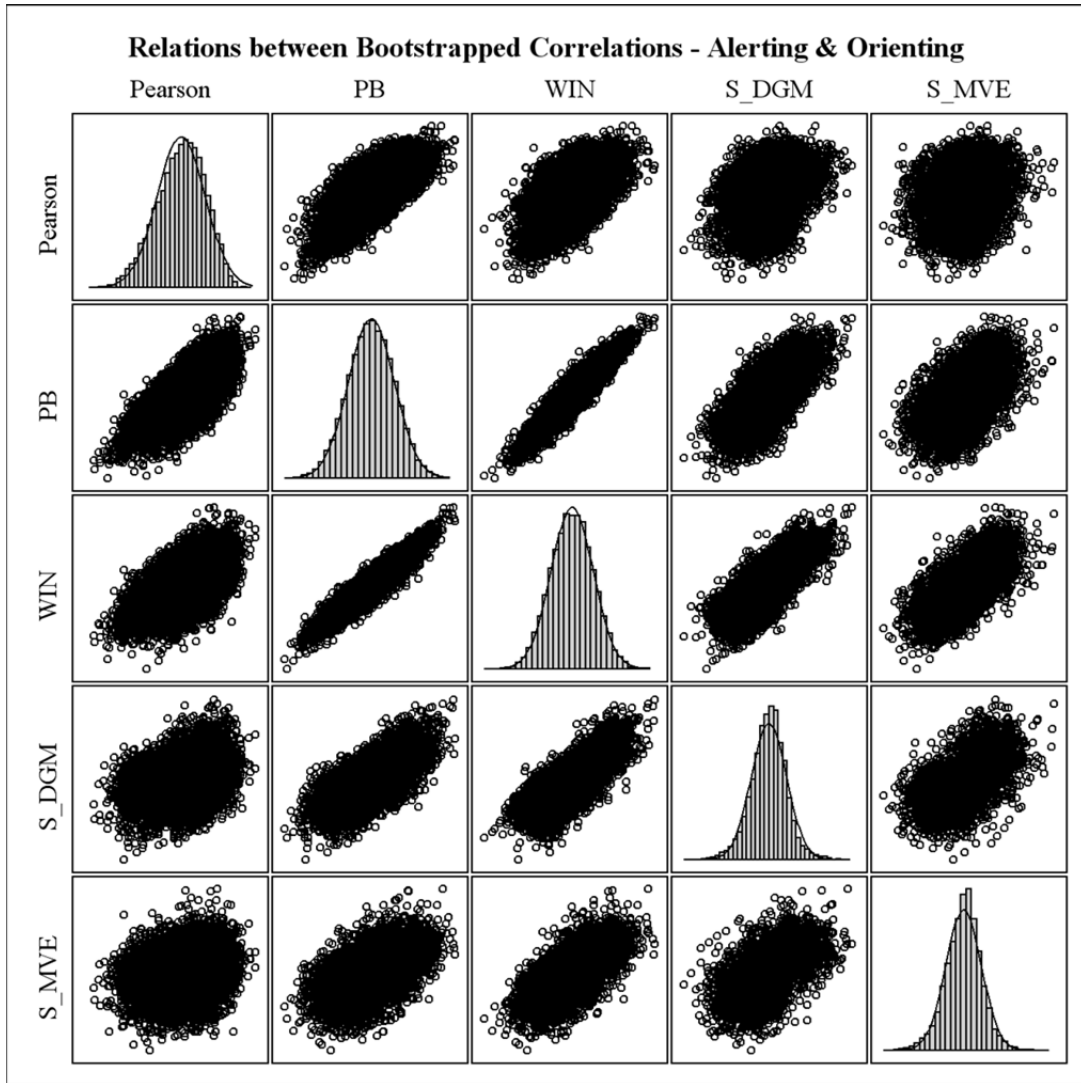


Fig 3. Scatterplot matrix demonstrating relations between five bootstrapped estimators of population correlations (the Pearson correlation, percentage bend correlation [PB], Winsorized correlation [WIN], skipped correlation using Donoho-Gasko median [S_DGM], skipped correlation using MVE [S_MVE]) for alerting and orienting. Histograms represent distributions of five correlation estimates derived from the 10000 bootstrapped samples.

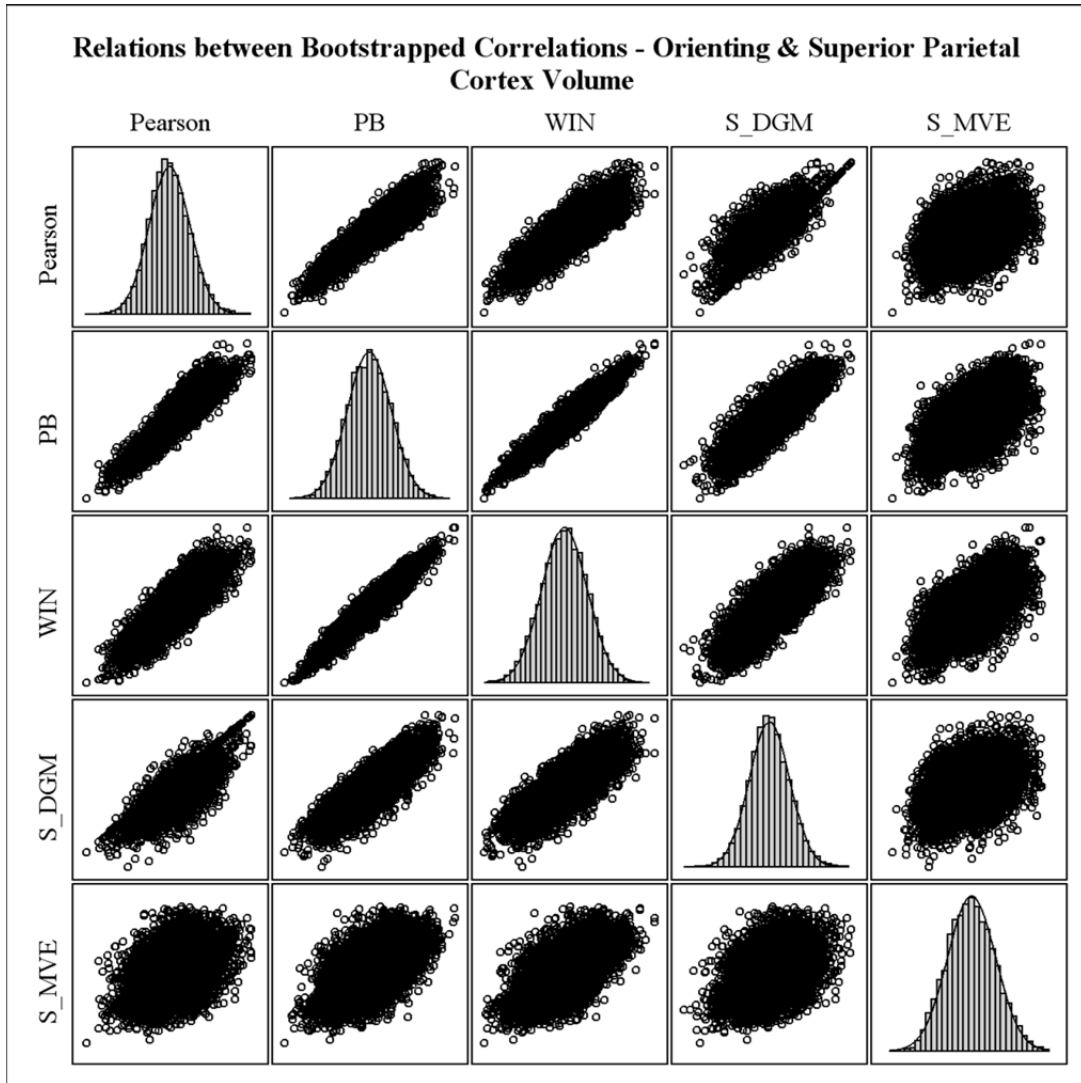


Fig 4. Scatterplot matrix demonstrating relations between five bootstrapped estimators of population correlations (the Pearson correlation, percentage bend correlation [PB], Winsorized correlation [WIN], skipped correlation using Donoho-Gasko median [S_DGM], skipped correlation using MVE [S_MVE]) for orienting and the superior parietal cortex volume. Histograms represent distributions of five correlation estimates derived from the 10000 bootstrapped samples.

The emergence of several patterns of relation among the five estimates across the different behavior-behavior and structure-function relations raises the possibility that characteristics of the univariate and multivariate distributions predict the pattern of relations across the different estimators. Characteristics of the multivariate distributions (Mardia & Foster, 1983) that might have affected the pattern of results across the five estimators were examined descriptively utilizing bubble plots. Figures 5a – 5d demonstrate the relations between the Pearson correlation and each of the four robust estimators and the impact of multivariate kurtosis on these relations. Specifically, in Figures 5a-d the mean value of the Pearson correlation was plotted against the mean of the four robust correlations for each of the behavior-behavior and structure-function relations. The size of the circle used to represent each behavior-behavior and structure-function relation in the plot reflects the degree of multivariate kurtosis or skewness in the parent relation. Larger circles represented larger values of kurtosis or skewness. All bubble plots indicated that the Pearson correlation was highly correlated with the percentage bend, Winsorized, and skipped correlation using Donoho-Gasko median for behavior-behavior and structure-function relations. At the same time the Pearson correlation was not related to the skipped correlation using MVE. Furthermore, the degree of multivariate kurtosis and skewness did not seem to impact the degree of relatedness between the Pearson correlation and the robust estimators. Consequently, differences across the five estimators did not appear to be strongly driven by departure of the joint distributions from multivariate normality.

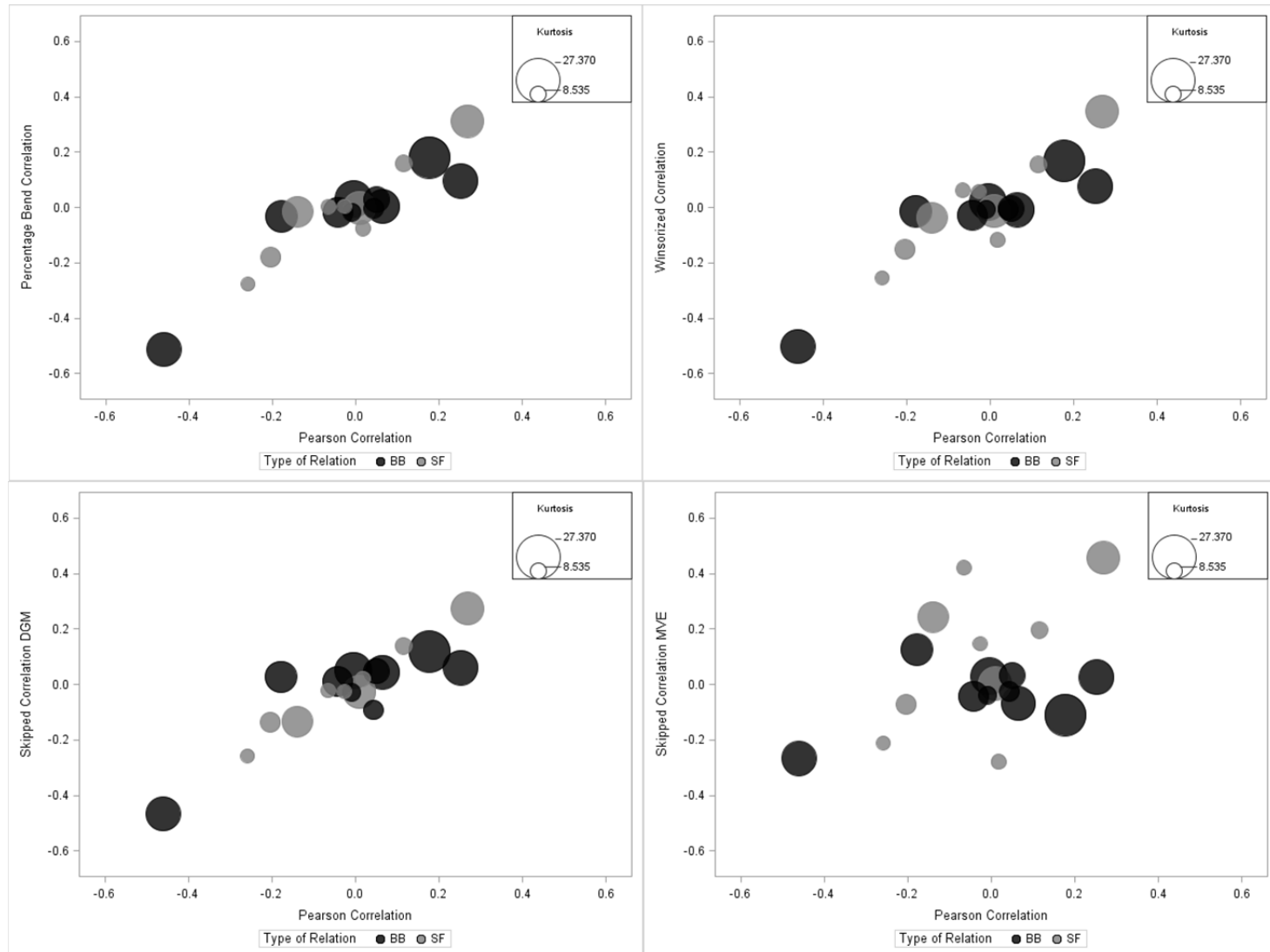


Fig 5a – 5d. Bubble plots demonstrating relations between multivariate kurtosis and estimates of correlation. Black bubbles represent behavior-behavior relations [BB], grey bubbles represent behavior-behavior relations [SF]. The mean of the bootstrapped estimate of Pearson correlation is plotted on the X axis, whereas the mean of the bootstrapped estimate of robust correlations is

Spina Bifida Group. The performance of five estimators in the spina bifida group was compared based on summary statistics (the mean, standard deviation, confidence intervals) computed on the set of bootstrapped replicates. Three distinguishable patterns of relations between means of bootstrapped estimators (Appendix C) were observed: (1) all estimators performed similarly, in sense their magnitude was comparable, (2) the Pearson estimate differed from the four robust estimators, i.e., the Pearson correlation was larger than the other estimators (the pattern was only found in behavior-behavior relations) (3) the skipped correlation using MVE differed from the other three robust estimators, which were comparable to the Pearson estimate. More specifically, the skipped correlation using MVE was higher for the structure-function relations and lower for the behavior-behavior relations. With regards to standard deviations (Appendix D) and confidence intervals based on percentiles (Appendix E) one pattern was observed. In particular, the standard deviations for the skipped correlation using MVE were higher than the standard deviations of other estimators. Consequently, the confidence intervals for skipped correlations using MVE were much wider compared to the confidence intervals for other estimates. Because of insufficient variability for certain measures computation of summary statistics for some estimators was not always possible. Overall, the patterns found in summary statistics of bootstrapped estimates of population correlations were consistent with the patterns observed in the single sample estimates.

Associations among the five estimators were examined using scatter plot matrices (see Appendix F) and revealed high correlations between the Pearson correlation estimates and the percentage bend and Winsorized correlations. Additionally, the Winsorized correlation was highly correlated with the percentage bend and skipped correlation using Donoho-Gasko

median. Lastly, the percentage bend correlation was strongly related to the skipped correlation using Donoho-Gasko median. At the same time, the skipped correlation using MVE did not seem to be highly correlated with other robust estimators nor with the Pearson correlation.

For the structure-function relations, associations between the five estimators revealed high correlations between the Pearson, percentage bend, Winsorized, and skipped correlation using Donoho-Gasko median. Additionally, the Winsorized, percentage bend, and skipped correlation using Donoho-Gasko median were highly correlated. Lastly, the percentage bend correlation was strongly related to the skipped correlation using Donoho-Gasko median. At the same time, skipped correlation using MVE did not seem to be highly correlated with other robust estimators and the Pearson correlation. Appendix G demonstrates relations between the five estimators for a specific pair of behavioral and brain measures.

Appendix H demonstrates the impact of multivariate kurtosis and skew on differences across the five estimators. Multivariate kurtosis and skewness did not appear to affect the relations across the different estimates, just as was seen in the total groups analysis.

Normal Controls. Due to small sample size and/or insufficient variability in some measures computation of summary statistics in the normal control sample was not always possible. Bootstrapped replicates computed on the normal controls sample were compared with respect to their means, standard deviations, and confidence intervals. Overall, the Pearson, Winsorized, and percentage bend correlation yielded similar mean values across the bootstrap samples (Appendix I). A similar pattern was found with regards to standard deviations (Appendix J) and confidence intervals based on percentiles (Appendix K). In

particular, standard deviations and confidence intervals were comparable for bootstrapped replicates of these three estimators.

For any given pair of variables in the behavior-behavior and structure-function relations, the Pearson, percentage bend, and Winsorized correlations were highly correlated across the 10,000 bootstrap samples. Appendices L and M demonstrate relations between these three estimators for a specific pair of variables.

Examination of relations between characteristics of multivariate distributions and differences across the five estimators revealed that multivariate kurtosis and skewness did not affect the relations among the Pearson, percentage bend, and Winsorized correlations (Appendix N).

Discussion

The present study focused on examination of the most common factors affecting estimation of Pearson's correlation coefficient while investigating structure-function and behavior-behavior relations in a small clinical sample. Four robust measures of correlation (the percentage bend correlation, Winsorized correlation, skipped correlation using the DGM, and skipped correlation using MVE) were applied in order to correct for the problems related to violations of statistical assumptions, which prevent accurate estimation using the Pearson correlation. Subsequently, structure-function and behavior-behavior relations in the domain of attention in the spina bifida, healthy controls, and total samples (spina bifida and normal controls) were investigated in order to expand the knowledge regarding attentional profile in spina bifida and typically developing children. More specifically, we examined relations between sustained attention, attentional control, three attention networks (alerting, orienting, conflict resolution), and volumetric brain measures derived from MRI.

Additionally, we investigated relations between the different types of attention and attention networks listed above.

Patterns of performance

In terms of patterns of performance regarding single sample as well as mean bootstrapped estimates of population correlation, distinct patterns of associations were observed in the total samples and spina bifida group for different pairs of variables. The first pattern suggested that all estimators performed similarly, whereas the second pattern indicated that the skipped correlation using MVE differed from the other three robust estimators, which were comparable to the Pearson's estimate.

Similar performance across the five estimators, which was found in pairs of variables with fewer univariate outliers and slight shifts from normality in marginal distributions, suggests that violations of distributional assumptions might have differentially affected the performance of the different estimators. In particular, slight shifts in marginal distributions might not distort Pearson's correlation as much as it would be expected based on previous findings (Heritier et al., 2009; Wilcox, 2005, Wilcox, 2008; Wilcox, 2010). Although there may be alternative explanations, it is possible that only highly skewed distributions with heavy tails significantly affect Pearson's correlation resulting in biased estimation of the Pearson's population correlation.

In terms of the second pattern of performance, dissimilarities in the magnitude of skipped correlation using MVE and the other three robust estimators as well as the Pearson's estimate were the most pronounced in the pairs of variables where at least one measure had a large amount of univariate outliers. Lack of similarities between the skipped correlation using MVE and other estimators might be related to the outlier detection method. More

specifically, the MVE outlier detection method tends to have a higher outside rate per observation compared to other robust measures of correlations which take into account the overall structure of the data (Wilcox, 2010). The outside rate per observation is associated with the anticipated amount of outliers in a random sample of size n (Wilcox, 2008). When an estimator has a high outside rate per observation, points that are not classified as outliers under univariate normality become flagged as outliers once the MVE outlier detection method is applied (Wilcox, 2010). Since the MVE outlier detection method has relatively high outside rate per observation, more than the necessary number of points is flagged as outliers, decreasing the number of points used in the estimation of population correlation. In particular, the population correlation is estimated using only the central 50% of the data, which in turn affects an accurate estimation of the population correlation. It is noteworthy that by setting the amount of Winsorizing to 0.5, Winsorized correlation and the skipped correlation using MVE might perform similarly in situations where many univariate and multivariate outliers are present. Although there may be alternative explanations, it seems that the skipped correlation using MVE performs differently than the Pearson's correlation, percentage bend correlation, Winsorized correlation, and skipped correlation using DGM when a large number of outliers is present. More specifically, the MVE outlier detection method not only flags univariate but also multivariate outliers decreasing the amount of data used in estimating the population correlation. Therefore, under certain conditions it might be advantageous to utilize the skipped correlation using DGM opposed to the skipped correlation using MVE and other robust correlations, because the skipped correlation using DGM not only accounts for the overall structure of the data (Wilcox, 2005; unlike the

percentage bend correlation or Winsorized correlation), but also has a relatively low outside rate per observation.

In addition to the patterns of relations described above, there was a third, distinct pattern of performance observed only in the spina bifida group. In particular, the Pearson's estimate differed from the four robust estimators, meaning the magnitude of the Pearson's estimate was higher compared to other estimators. Lack of robustness of the Pearson's correlation is well documented in the statistical literature (Cohen et al., 2003; Hays, 1994; Wilcox, 1990; Wilcox, 2005). The estimation of population correlation might be affected when variables are not normally distributed and outliers are present. It is noteworthy that depending on the degree of non-normality combined with the presence of multiple outliers, estimation of Pearson's population correlation is differently affected. More specifically, slight to moderate shifts in the marginal distributions do not always result in a distorted view of correlations as it was shown at the beginning of the discussion regarding the first pattern of performance. Although there may be alternative explanations, it seems that in situations where at least one variable is heavy tailed and the other has multiple outliers, the estimation of Pearson's population correlation is more affected compared to the situation where at least one variable is highly skewed and the other has multiple outliers.

With regards to normal controls, different patterns of performance were found with regards to single sample estimates and mean bootstrapped estimates of population correlation. In particular, the skipped correlation using MVE differed from other three robust estimators, which were comparable to the Pearson's estimate in the single sample estimate. At the same time, all estimators performed similarly in the bootstrapped estimate of population correlation. Lack of consistent findings can be attributed to problems encountered

estimating the skipped correlation using the bootstrap. Due to the small sample size in the control sample and limited variability in some measures, singular covariance matrices were returned for many bootstrap samples. In these instances, estimation of the skipped correlation using MVE or DGM is not possible, because MVE or DGM outlier detection methods involve inversion of the covariance matrix (van der Linde & Houle, 2006).

Differences in the patterns of performance in the total groups and within groups analyses can be attributed to the phenomenon known as the group structure to the data, which results from the inclusion of heterogeneous subgroups in the study population. The presence of group structure in the data can significantly distort the correlation between two measures. Ignoring the group structure to the data might result in underestimation or overestimation of the correlation. Therefore, the pattern of performance which was apparent in the spina bifida group might have been masked in the mixed sample. In other words, the pattern of performance might be affected by the presence or absence of spina bifida, which is associated with certain brain malformations and attention deficits. However, given predominance of spina bifida group in the total samples, the group structure to the data does not seem to greatly influence patterns of performance among various estimators.

Relations between bootstrapped correlations

Examination of relations between five correlations computed on a given pair of variables on each of the 10,000 bootstrap samples suggested strong associations between the Pearson's correlation and the percentage bend as well as Winsorized correlations. Obtained results are consistent with previous findings (Wilcox, 1994; Wilcox, 1997; Wilcox, 2003; Wilcox, 2005; Wilcox, 2008) suggesting that all of those types of correlations estimate the degree of linear relation between two measures. Under normality the percentage bend and Winsorized

correlations give similar estimates to the Pearson's correlation. More specifically, when variables are independent the coefficients of robust correlations and Pearson's correlation are equal to 0. Consequently, when variables are perfectly dependent the coefficients of robust correlations and Pearson's correlation are equal to 1. Therefore, robust correlations might have comparable interpretations to the Pearson's correlation, however there are advantageous when confronted with outliers and non-normality (King, 2003).

In consistency with the literature, high correlations were found between the percentage bend and Winsorized correlations (Wilcox, 1997; Wilcox, 2003; Wilcox, 2005). The percentage bend and Winsorized correlations are both robust measures of correlation, which are less sensitive to violations of distributional assumptions and presence of outliers. Both of those measures do not take into account overall structure of the data, meaning they help in guarding against outliers in univariate but not in multivariate distributions. In the present study the breakdown point of both correlations was set to 0.2, allowing for maximum 20% of model misspecification before estimation bias is too high (Heritier et al., 2009). Finally both of those correlations refer directly or indirectly to the Pearson's estimate. In particular, the percentage bend correlation is a modification of the Pearson's correlation, whereas the Winsorized correlation computes the Pearson's correlation after Winsorizing the data, i.e., trimming the extreme observations and replacing them with adjacent values. In sum, the percentage bend and Winsorized correlations share many properties which might explain high correlations between those estimators across a wide variety of behavior-behavior and structure-function relations in this study.

Interestingly, the percentage bend and Winsorized correlations were highly correlated with the skipped correlation using DGM. The main advantage of the skipped correlation

using DGM over the percentage bend and Winsorized correlations is that the former one utilizes multivariate outlier detection method, which takes into account the overall structure of the data, as well as has the highest possible breakdown point (0.5). Given distinguishable properties between the skipped correlation using DGM, and the percentage and Winsorized correlations, it is rather surprising that those measures are highly correlated with each other. One possible explanation is that in situation where only univariate outliers are present those correlations will give comparable estimates. Additionally, the skipped correlation using DGM utilizes the projection method based on the multivariate median, and the modified boxplot rule in order to detect outliers (Wilcox, 2003; Wilcox, 2005). The boxplot is a useful tool in detecting univariate outliers. Despite using the multivariate median, the DGM outlier detection method is only partly multivariate, which might bring some similarities between the skipped correlation using DGM, and percentage bend and Winsorized correlations.

Lastly, skipped correlation using MVE was not highly correlated with robust estimators and Pearson's correlation. Although there may be alternative explanations, lack of correlations between the skipped correlation using MVE and other estimates of correlation can be attributed to the MVE outlier detection method, which decreases by 50% the number of points used in computation of Pearson's correlation. More specifically, unlike other robust estimates of correlation, the skipped correlation using MVE is computed only on 50% of the original data. Consequently, the Pearson's correlation computed on the remaining data gives a poor estimate of the population Pearson's correlation. Discarding outliers using the MVE outlier detection method, and then computing Pearson's correlation on the remaining data might affect accurate estimation of Pearson's population correlation.

Structure-function and behavior-behavior relations

In the total samples and spina bifida group, the only statistically significant correlation across all estimators was found for sustained attention and attentional control. This finding is concordant with those of Manly et al. (2001) showing a negative correlation between sustained attention and attentional control measures. Weak correlations between attentional networks are consistent with literature findings postulating independence of those networks (Fan et al., 2002; Rueda et al., 2004). Furthermore, independence of attentional networks and other behavioral measures suggests that different types of attention are independent constructs, which refer to distinct cognitive processes despite involving overlapping brain measures (Posner & Petersen, 1990; Ward, 2004). Finally, lack of statistically significant structure-function relations might be attributed to complexity of attentional processes, which are controlled by various, interrelated brain structures (Posner, 1984; Posner & Petersen, 1990), and therefore it might be difficult to capture structure-function relations utilizing isolated brain structures.

No statistically significant correlations were found in the normal controls. Beside substantive explanations provided above, lack of statistically significant correlations in healthy controls might be attributed to small sample size, and therefore low power to detect statistically significant associations.

Conclusions

Using alternative approaches to estimate relations can assist investigators when confronted with small samples and multivariate non-normal data. Utilization of the Pearson correlation along with robust correlations can strengthen inferences about variable relations. Using the bootstrap to obtain empirical distributions for the estimates can further strengthen

conclusions about variable relations. The similarity of estimates across methods suggested that the lack of structure-function relations found in the literature is not easily attributed to violations of distributional assumptions.

Limitations

Possible limitations of the study include selection of default parameters, as well as applying investigated methods only to one clinical population. It might be useful to examine the pattern of relations using different parameters in order to further understand relations between different correlational measures. Additionally, application of the investigated methods into different clinical populations might help in assessing usefulness of selected measures in a wider context.

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Appendix A

Single sample estimates of population correlation for behavior-behavior and structure-function relations (Spina bifida group)

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
<i>Alerting-Sustained Attention</i>	-0.042	0.050	0.040	0.097	0.036
Alerting-Conflict Resolution	0.015	0.034	-0.006	0.034	0.122
Alerting-Attentional Control	0.097	0.037	0.027	-0.058	-0.026
Alerting-Orienting	0.304**	0.121	0.112	0.101	0.101
Sustained Attention-Attentional Control	-0.387**	-0.431***	-0.428***	-0.370*	-0.368
Conflict Resolution-Sustained Attention	0.106	0.034	0.024	0.066	0.054
Conflict Resolution-Attentional Control	-0.053	-0.090	-0.064	-0.121	-0.160
<u>Orienting-Sustained Attention</u>	<u>0.183</u>	<u>0.226*</u>	<u>0.206</u>	<u>0.141</u>	<u>-0.004</u>
Orienting-Conflict Resolution	-0.219*	-0.064	-0.048	0.037	-0.001
Orienting-Attentional Control	-0.052	-0.019	0.005	-0.074	-0.123
Alerting-Right Inferior Parietal Lobe	0.098	0.110	0.119	0.098	0.016
Alerting-Thalamus	0.040	-0.113	-0.140	0.040	-0.253
Sustained Attention-Anterior Cingulate Cortex	0.001	-0.111	-0.181	0.001	NA
<u>Sustained Attention-Dorsolateral Prefrontal Cortex</u>	<u>-0.293</u>	<u>-0.198</u>	<u>-0.235</u>	<u>-0.301</u>	<u>-0.673</u>
Conflict Resolution-Anterior Cingulate Cortex	-0.284	-0.317*	-0.312*	-0.284	-0.250
Conflict Resolution-Dorsolateral Prefrontal Cortex	-0.208	-0.155	-0.127	-0.031	-0.205
Attentional Control-Anterior Cingulate Cortex	-0.071	-0.010	0.048	0.024	NA
<i>Attentional Control-Dorsolateral Prefrontal Cortex</i>	0.035	0.006	0.034	0.009	-0.057
Orienting-Superior Parietal Cortex	0.010	0.019	0.051	0.010	0.152
Orienting-Thalamus	0.288	0.326*	0.367*	0.288	0.470

Note. Behavior-Behavior Relations N = 82; Structure-Function Relations N = 43

*** p < .001. ** p < .01. * p < .05.

NA - Insufficient variability in order to use the estimator

Italic - Estimators perform similarly

Bolded - the Pearson estimate differs from the four robust estimators

Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate

Appendix B

Single sample estimates of population correlation for behavior-behavior and structure-function relations (Normal Controls)

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
Alerting-Sustained Attention	-0.364	-0.387*	-0.393*	-0.142	-0.331
Alerting-Conflict Resolution	0.420*	0.207	0.203	0.091	0.415
Alerting-Attentional Control	0.328	0.287	0.294	0.345	0.494
<u>Alerting-Orienting</u>	<u>0.009</u>	<u>-0.066</u>	<u>-0.041</u>	<u>-0.150</u>	<u>-0.374</u>
Sustained Attention-Attentional Control	-0.578***	-0.436*	-0.429*	-0.343	-0.057
Conflict Resolution-Sustained Attention	0.022	-0.055	-0.062	-0.130	-0.259
Conflict Resolution-Attentional Control	0.007	0.005	0.002	0.122	-0.210
Orienting-Sustained Attention	-0.095	-0.163	-0.170	-0.381	-0.057
Orienting-Conflict Resolution	0.048	0.163	0.153	0.450*	0.197
Orienting-Attentional Control	0.205	0.223	0.207	0.207	0.715
Alerting-Right Inferior Parietal Lobe	-0.037	-0.044	0.094	-0.037	0.154
Alerting-Thalamus	-0.156	-0.166	-0.153	-0.156	-0.250
Sustained Attention-Anterior Cingulate Cortex	0.311	0.331	0.300	0.240	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	0.347	0.354	0.288	0.347	0.189
Conflict Resolution-Anterior Cingulate Cortex	-0.155	-0.177	-0.131	-0.471	0.562
<u>Conflict Resolution-Dorsolateral Prefrontal Cortex</u>	<u>-0.228</u>	<u>-0.166</u>	<u>-0.221</u>	<u>-0.228</u>	<u>0.632</u>
Attentional Control-Anterior Cingulate Cortex	-0.066	0.172	0.154	0.138	NA
Attentional Control-Dorsolateral Prefrontal Cortex	-0.128	0.044	0.135	-0.128	0.330
Orienting-Superior Parietal Cortex	0.003	-0.029	-0.076	-0.152	0.084
Orienting-Thalamus	0.117	0.125	0.167	0.117	-0.046

Note. Behavior-Behavior Relations N = 29; Structure-Function Relations N = 18

*** p < .001. ** p < .01. * p < .05.

NA - Insufficient variability in order to use the estimator

Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate

Appendix C

Mean Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Spina Bifida Group)

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
Alerting-Sustained Attention	-0.026	0.046	0.036	0.070	0.115
<i>Alerting-Conflict Resolution</i>	<i>0.013</i>	<i>0.025</i>	<i>0.007</i>	<i>0.047</i>	<i>0.076</i>
Alerting-Attentional Control	0.095	0.039	0.027	-0.045	-0.032
Alerting-Orienting	0.271	0.117	0.104	0.108	0.097
Sustained Attention-Attentional Control	-0.392	-0.425	-0.422	-0.379	-0.340
Conflict Resolution-Sustained Attention	0.097	0.031	0.018	0.064	-0.039
Conflict Resolution-Attentional Control	-0.054	-0.082	-0.067	-0.099	-0.079
<u>Orienting-Sustained Attention</u>	<u>0.191</u>	<u>0.218</u>	<u>0.210</u>	<u>0.151</u>	<u>0.065</u>
Orienting-Conflict Resolution	-0.204	-0.066	-0.046	0.016	0.057
Orienting-Attentional Control	-0.052	-0.019	-0.006	-0.020	-0.064
Alerting-Right Inferior Parietal Lobe	0.100	0.115	0.122	0.103	0.177
<u>Alerting-Thalamus</u>	<u>0.027</u>	<u>-0.099</u>	<u>-0.139</u>	<u>0.027</u>	<u>-0.283</u>
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	NA	NA	NA	NA	NA
Conflict Resolution-Anterior Cingulate Cortex	-0.286	-0.313	-0.311	-0.284	-0.293
Conflict Resolution-Dorsolateral Prefrontal Cortex	-0.198	-0.150	-0.148	-0.076	-0.161
Attentional Control-Anterior Cingulate Cortex	-0.069	-0.016	0.040	-0.037	0.347
Attentional Control-Dorsolateral Prefrontal Cortex	0.031	0.011	0.027	0.004	0.017
<i>Orienting-Superior Parietal Cortex</i>	<i>0.019</i>	<i>0.024</i>	<i>0.027</i>	<i>0.006</i>	<i>0.022</i>
Orienting-Thalamus	0.281	0.319	0.353	0.290	0.473

Note. Behavioral Relations N = 82; Structure-Function Relations N = 43

NA - Insufficient variability or sample size is too small in order to use estimators

Italic - Estimators perform similarly (the first pattern)

Bolded - the Pearson estimate differs from the four robust estimators (the second pattern)

Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate (the third pattern)

Appendix D

Standard Deviations of Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Spina Bifida Group)

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
Alerting-Sustained Attention	0.140	0.114	0.112	0.121	0.200
Alerting-Conflict Resolution	0.142	0.119	0.117	0.153	0.195
Alerting-Attentional Control	0.109	0.119	0.120	0.167	0.206
Alerting-Orienting	0.187	0.124	0.118	0.182	0.218
Sustained Attention-Attentional Control	0.084	0.090	0.094	0.097	0.203
Conflict Resolution-Sustained Attention	0.097	0.111	0.112	0.106	0.183
<u>Conflict Resolution-Attentional Control</u>	<u>0.094</u>	<u>0.114</u>	<u>0.114</u>	<u>0.132</u>	<u>0.253</u>
Orienting-Sustained Attention	0.088	0.104	0.111	0.104	0.245
Orienting-Conflict Resolution	0.119	0.114	0.114	0.128	0.206
Orienting-Attentional Control	0.116	0.117	0.120	0.154	0.226
Alerting-Right Inferior Parietal Lobe	0.129	0.144	0.156	0.130	0.281
Alerting-Thalamus	0.169	0.163	0.166	0.172	0.249
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	NA	NA	NA	NA	NA
Conflict Resolution-Anterior Cingulate Cortex	0.098	0.135	0.148	0.100	0.291
Conflict Resolution-Dorsolateral Prefrontal Cortex	0.189	0.162	0.157	0.186	0.357
Attentional Control-Anterior Cingulate Cortex	0.205	0.186	0.178	0.221	0.380
Attentional Control-Dorsolateral Prefrontal Cortex	0.157	0.158	0.155	0.170	0.297
<u>Orienting-Superior Parietal Cortex</u>	<u>0.119</u>	<u>0.152</u>	<u>0.160</u>	<u>0.120</u>	<u>0.341</u>
Orienting-Thalamus	0.152	0.154	0.159	0.156	0.319

Note. Behavioral Relations N = 82; Structure-Function Relations N = 43

NA - Insufficient variability or sample size is too small in order to use estimators

Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate

Appendix E

Confidence Interval of Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Spina Bifida Group)

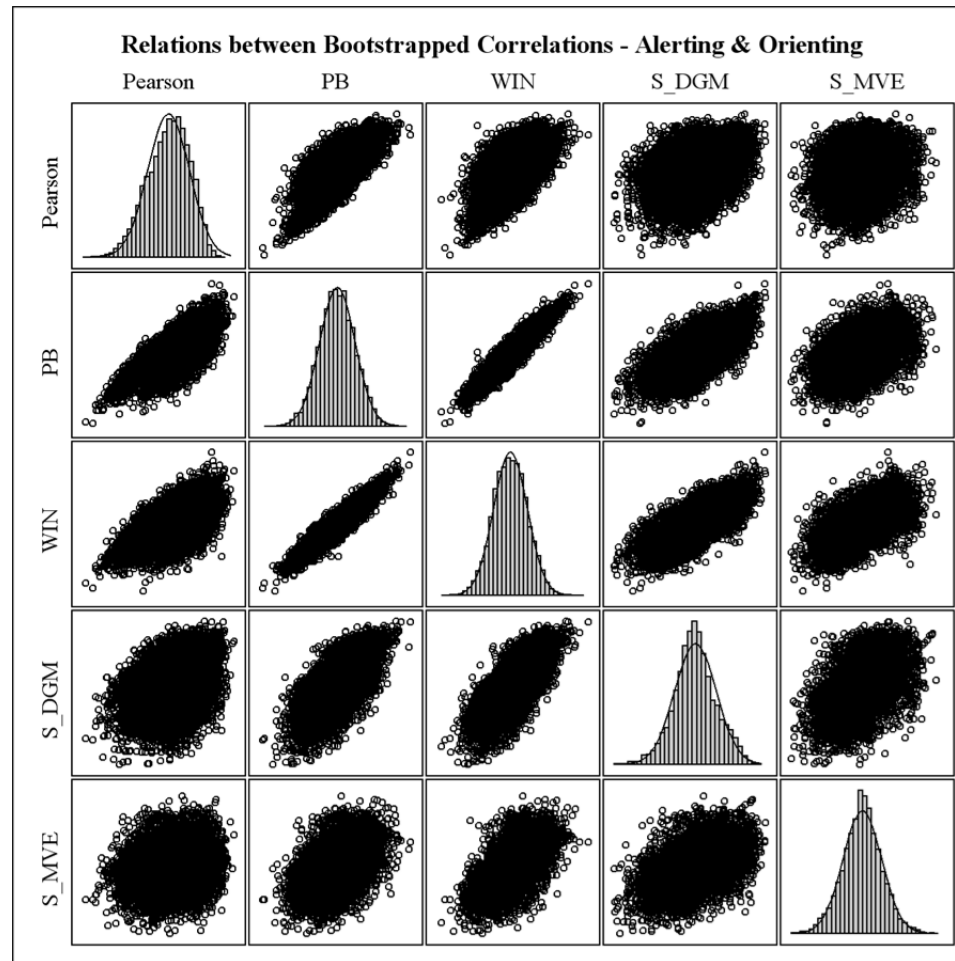
Pair of Variables	Pearson Correlation		Percentage Bend Correlation		Winsorized Correlation		Skipped Correlation using Donoho-Gasko Median		Skipped Correlation using MVE	
	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)
Alerting-Orienting	-0.057	0.555	-0.085	0.321	-0.089	0.300	-0.193	0.427	-0.269	0.453
Alerting-Conflict Resolution	-0.217	0.251	-0.172	0.221	-0.183	0.204	-0.211	0.295	-0.245	0.394
<u>Alerting-Sustained Attention</u>	<u>-0.245</u>	<u>0.213</u>	<u>-0.145</u>	<u>0.232</u>	<u>-0.150</u>	<u>0.217</u>	<u>-0.132</u>	<u>0.269</u>	<u>-0.214</u>	<u>0.436</u>
Alerting-Attentional Control	-0.092	0.266	-0.155	0.233	-0.172	0.223	-0.312	0.234	-0.379	0.310
Orienting-Conflict Resolution	-0.381	0.012	-0.252	0.122	-0.233	0.145	-0.201	0.220	-0.289	0.394
Orienting-Sustained Attention	0.056	0.348	0.041	0.383	0.024	0.386	-0.013	0.330	-0.332	0.486
Orienting-Attentional Control	-0.252	0.132	-0.210	0.175	-0.202	0.194	-0.283	0.223	-0.448	0.302
Conflict Resolution-Sustained Attention	-0.077	0.242	-0.152	0.214	-0.165	0.201	-0.115	0.235	-0.350	0.256
Conflict Resolution-Attentional Control	-0.206	0.105	-0.268	0.108	-0.253	0.121	-0.306	0.130	-0.466	0.383
Sustained Attention-Attentional Control	-0.530	-0.252	-0.565	-0.271	-0.570	-0.260	-0.535	-0.216	-0.634	0.052
Orienting-Superior Parietal Cortex	-0.161	0.228	-0.225	0.278	-0.240	0.283	-0.178	0.216	-0.531	0.619
<u>Orienting-Thalamus</u>	<u>-0.003</u>	<u>0.501</u>	<u>0.057</u>	<u>0.559</u>	<u>0.076</u>	<u>0.598</u>	<u>0.002</u>	<u>0.518</u>	<u>-0.178</u>	<u>0.830</u>
Alerting-Thalamus	-0.266	0.295	-0.365	0.175	-0.410	0.140	-0.273	0.299	-0.693	0.130
Alerting-Right Inferior Parietal Lobe	-0.111	0.312	-0.126	0.348	-0.137	0.374	-0.109	0.315	-0.268	0.637
Conflict Resolution-Dorsolateral Prefrontal Cortex	-0.504	0.116	-0.414	0.122	-0.406	0.110	-0.410	0.204	-0.638	0.571
Conflict Resolution-Anterior Cingulate Cortex	-0.442	-0.123	-0.525	-0.085	-0.546	-0.061	-0.443	-0.115	-0.752	0.222
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Attentional Control-Anterior Cingulate Cortex	-0.398	0.277	-0.325	0.284	-0.259	0.321	-0.391	0.342	-0.395	0.841
Attentional Control-Dorsolateral Prefrontal Cortex	-0.237	0.279	-0.251	0.272	-0.228	0.283	-0.281	0.276	-0.504	0.472

Note. Behavioral Relations N = 82; Structure-Function Relations N = 43

NA - Insufficient variability or sample size is too small in order to use estimators

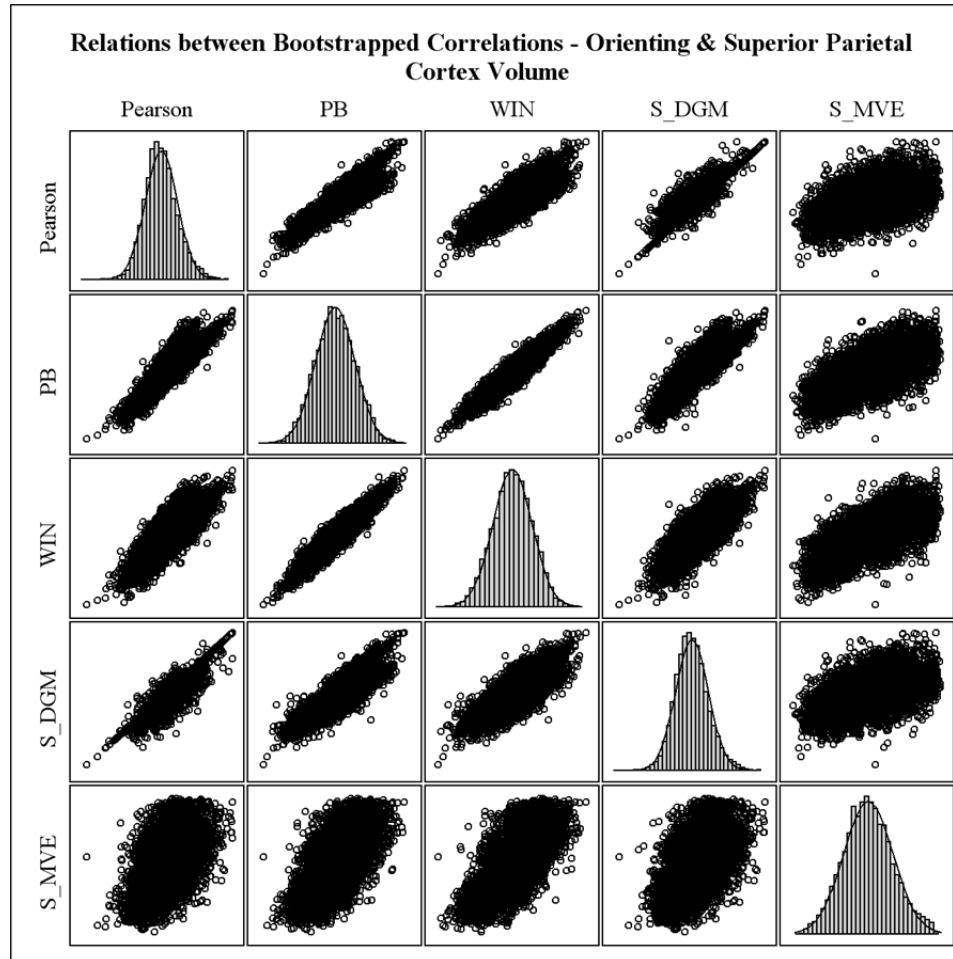
Underline - the Skipped correlation using MVE differs from the other three robust estimators, which are comparable to the Pearson estimate

Appendix F



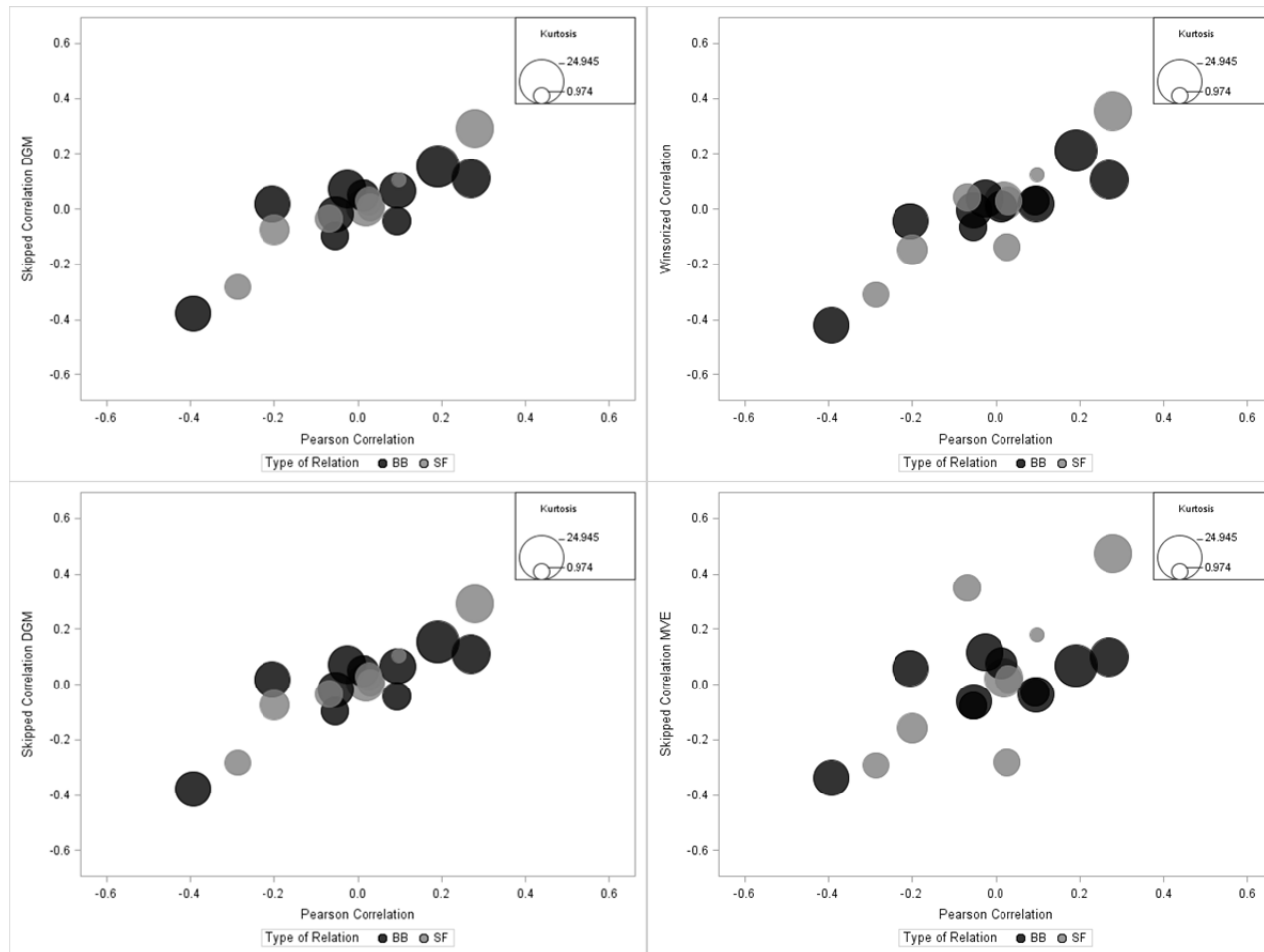
Scatterplot matrix demonstrating relations between five bootstrapped estimators of population correlations (the Pearson correlation, percentage bend correlation [PB], Winsorized correlation [WIN], skipped correlation using Donoho-Gasko median [S_DGM], skipped correlation using MVE [S_MVE]) for alerting and orienting in the spina bifida group. Histograms represent distributions of five correlation estimates derived from the 10000 bootstrapped samples.

Appendix G



Scatterplot matrix demonstrating relations between five bootstrapped estimators of population correlations (the Pearson correlation, percentage bend correlation [PB], Winsorized correlation [WIN], skipped correlation using Donoho-Gasko median [S_DGM], skipped correlation using MVE [S_MVE]) for orienting and the superior parietal in the spina bifida group. Histograms represent distributions of five correlation estimates derived from the 10000 bootstrapped samples.

Appendix H



Bubble plots demonstrating relations between multivariate kurtosis and estimates of correlation. Black bubbles represent behavior-behavior relations [BB], grey bubbles represent behavior-behavior relations [SF]. The mean of the bootstrapped estimate of Pearson correlation is plotted on the X axis, whereas the mean of the bootstrapped estimate of two robust correlations is plotted on the Y axis of four bubble plots.

Appendix I

Mean Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Normal Controls)

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
<i>Alerting-Sustained Attention</i>	-0.363	-0.370	-0.348	NA	NA
Alerting-Conflict Resolution	0.363	0.201	0.182	NA	NA
Alerting-Attentional Control	0.324	0.299	0.284	NA	NA
Alerting-Orienting	0.0005	-0.056	-0.038	NA	NA
Sustained Attention-Attentional Control	NA	NA	NA	NA	NA
Conflict Resolution-Sustained Attention	0.014	-0.039	-0.042	NA	NA
Conflict Resolution-Attentional Control	0.013	0.019	0.009	NA	NA
Orienting-Sustained Attention	-0.102	-0.144	-0.140	NA	NA
Orienting-Conflict Resolution	0.059	0.140	0.145	NA	NA
Orienting-Attentional Control	0.206	0.216	0.196	NA	NA
Alerting-Right Inferior Parietal Lobe	-0.028	-0.0004	0.052	NA	NA
<i>Alerting-Thalamus</i>	-0.165	-0.171	-0.186	NA	NA
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	NA	NA	NA	NA	NA
Conflict Resolution-Anterior Cingulate Cortex	-0.156	-0.160	-0.100	NA	NA
Conflict Resolution-Dorsolateral Prefrontal Cortex	-0.213	-0.149	-0.133	NA	NA
Attentional Control-Anterior Cingulate Cortex	-0.033	0.120	0.129	NA	NA
Attentional Control-Dorsolateral Prefrontal Cortex	-0.089	0.036	0.099	NA	NA
Orienting-Superior Parietal Cortex	-0.006	0.002	-0.014	NA	NA
Orienting-Thalamus	0.115	0.110	0.132	NA	NA

Note. Behavioral Relations N = 29; Structure-Function Relations N = 18

NA - Insufficient variability or sample size is too small in order to use the estimator

Italic - Estimators perform similarly

Appendix J

Standard Deviations of Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Normal Controls)

Pair of Variables	Pearson Correlation	Percentage Bend Correlation	Winsorized Correlation	Skipped Correlation using Donoho-Gasko Median	Skipped Correlation using MVE
Alerting-Sustained Attention	0.206	0.154	0.171	NA	NA
Alerting-Conflict Resolution	0.236	0.183	0.208	NA	NA
Alerting-Attentional Control	0.267	0.206	0.208	NA	NA
Alerting-Orienting	0.141	0.184	0.198	NA	NA
Sustained Attention-Attentional Control	NA	NA	NA	NA	NA
Conflict Resolution-Sustained Attention	0.168	0.192	0.196	NA	NA
Conflict Resolution-Attentional Control	0.164	0.181	0.193	NA	NA
Orienting-Sustained Attention	0.191	0.207	0.208	NA	NA
<i>Orienting-Conflict Resolution</i>	<i>0.217</i>	<i>0.219</i>	<i>0.212</i>	<i>NA</i>	<i>NA</i>
Orienting-Attentional Control	0.154	0.188	0.210	NA	NA
Alerting-Right Inferior Parietal Lobe	0.181	0.252	0.300	NA	NA
Alerting-Thalamus	0.171	0.228	0.272	NA	NA
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	NA	NA	NA	NA	NA
Conflict Resolution-Anterior Cingulate Cortex	0.240	0.291	0.324	NA	NA
Conflict Resolution-Dorsolateral Prefrontal Cortex	0.243	0.299	0.339	NA	NA
Attentional Control-Anterior Cingulate Cortex	0.210	0.242	0.263	NA	NA
<i>Attentional Control-Dorsolateral Prefrontal Cortex</i>	<i>0.234</i>	<i>0.247</i>	<i>0.270</i>	<i>NA</i>	<i>NA</i>
Orienting-Superior Parietal Cortex	0.220	0.270	0.299	NA	NA
Orienting-Thalamus	0.239	0.248	0.265	NA	NA

Note. Behavioral Relations N = 29; Structure-Function Relations N = 18

NA - Insufficient variability or sample size is too small in order to use the estimator

Italic - Estimators perform similarly

Appendix K

Confidence Interval of Bootstrapped Estimates of Population Correlation for Behavior-Behavior and Structure-Function Relations (Normal Controls)

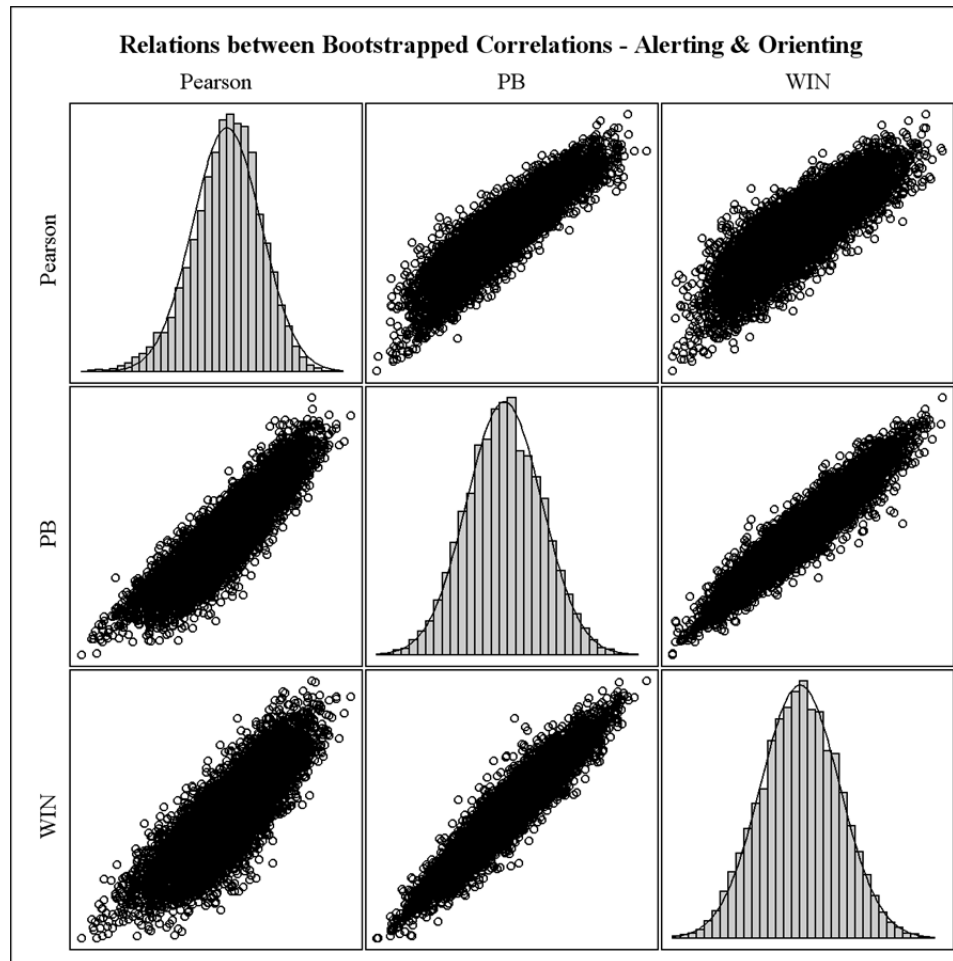
Pair of Variables	Pearson Correlation		Percentage Bend Correlation		Winsorized Correlation		Skipped Correlation using Donoho-Gasko Median		Skipped Correlation using MVE	
	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)	lower (2.5%)	upper (97.5%)
<i>Alerting-Orienting</i>	-0.251	0.217	-0.357	0.247	-0.371	0.287	NA	NA	NA	NA
Alerting-Conflict Resolution	-0.038	0.699	-0.103	0.495	-0.178	0.503	NA	NA	NA	NA
Alerting-Sustained Attention	-0.701	-0.033	-0.606	-0.101	-0.601	-0.042	NA	NA	NA	NA
Alerting-Attentional Control	-0.123	0.748	-0.057	0.624	-0.074	0.612	NA	NA	NA	NA
Orienting-Conflict Resolution	-0.296	0.419	-0.232	0.485	-0.218	0.484	NA	NA	NA	NA
Orienting-Sustained Attention	-0.419	0.213	-0.480	0.202	-0.473	0.211	NA	NA	NA	NA
Orienting-Attentional Control	-0.053	0.453	-0.103	0.518	-0.165	0.530	NA	NA	NA	NA
Conflict Resolution-Sustained Attention	-0.274	0.277	-0.354	0.280	-0.357	0.284	NA	NA	NA	NA
Conflict Resolution-Attentional Control	-0.252	0.284	-0.277	0.315	-0.307	0.323	NA	NA	NA	NA
Sustained Attention-Attentional Control	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Orienting-Superior Parietal Cortex	-0.369	0.350	-0.442	0.449	-0.511	0.479	NA	NA	NA	NA
<i>Orienting-Thalamus</i>	-0.281	0.507	-0.306	0.507	-0.322	0.542	NA	NA	NA	NA
Alerting-Thalamus	-0.448	0.108	-0.543	0.207	-0.619	0.274	NA	NA	NA	NA
Alerting-Right Inferior Parietal Lobe	-0.309	0.285	-0.415	0.414	-0.448	0.531	NA	NA	NA	NA
Conflict Resolution-Dorsolateral Prefrontal Cortex	-0.563	0.236	-0.604	0.383	-0.637	0.460	NA	NA	NA	NA
Conflict Resolution-Anterior Cingulate Cortex	-0.536	0.261	-0.594	0.353	-0.595	0.489	NA	NA	NA	NA
Sustained Attention-Anterior Cingulate Cortex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sustained Attention-Dorsolateral Prefrontal Cortex	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Attentional Control-Anterior Cingulate Cortex	-0.343	0.338	-0.285	0.509	-0.339	0.539	NA	NA	NA	NA
Attentional Control-Dorsolateral Prefrontal Cortex	-0.430	0.338	-0.364	0.456	-0.364	0.525	NA	NA	NA	NA

Note. Behavioral Relations N = 29; Structure-Function Relations N = 18

NA - Insufficient variability or sample size is too small in order to use the estimator

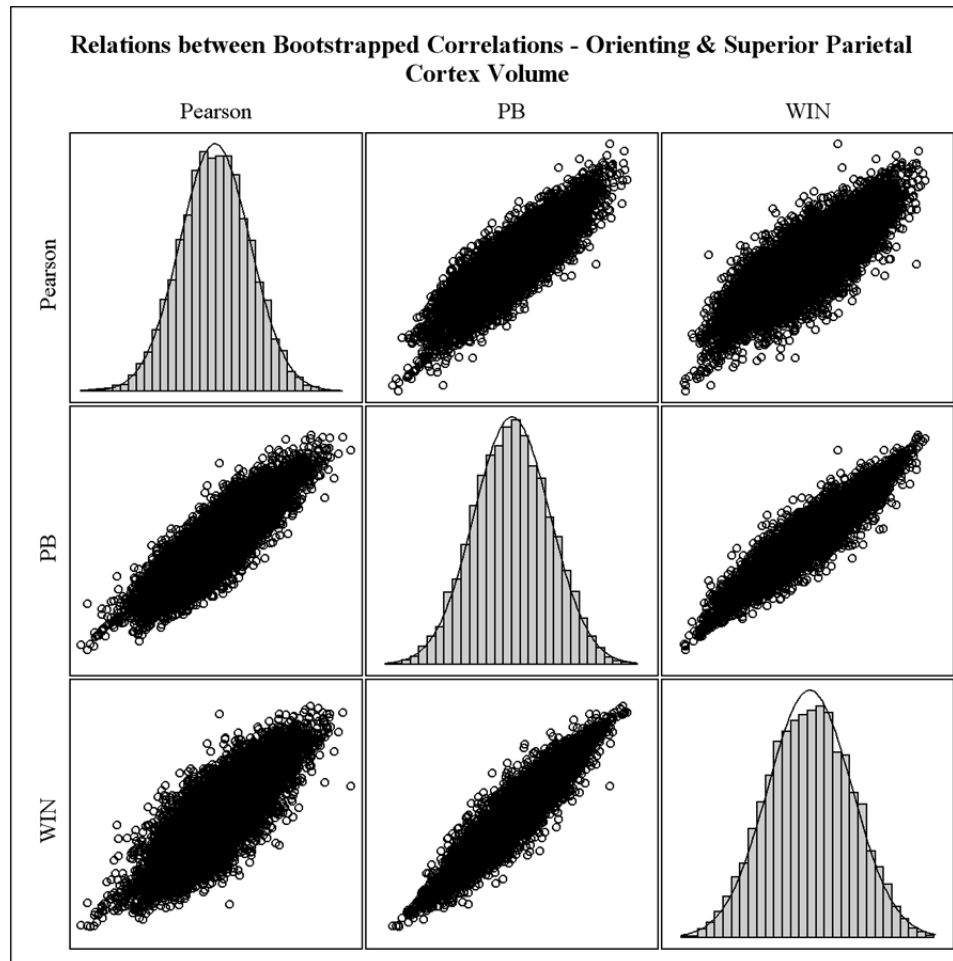
Italic - Estimators perform similarly

Appendix L



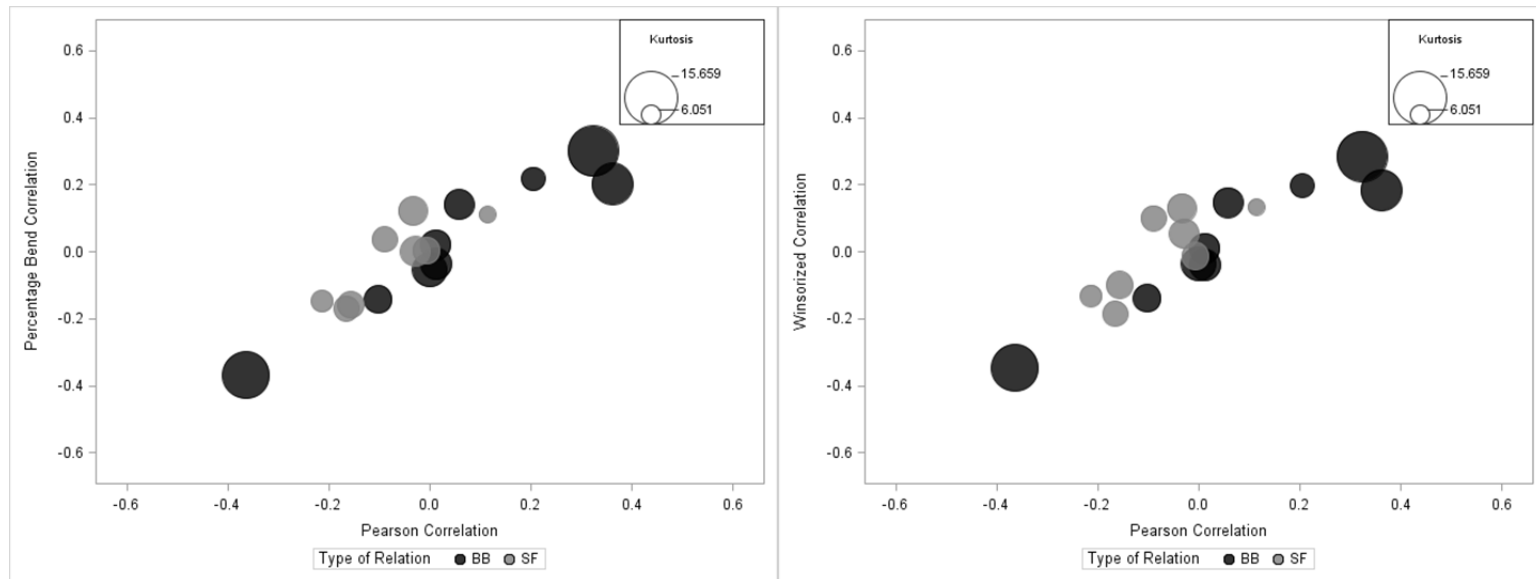
Scatterplot matrix demonstrating relations between five bootstrapped estimators of population correlations (the Pearson correlation, percentage bend correlation [PB], Winsorized correlation [WIN]) for alerting and orienting in the normal controls. Histograms represent distributions of five correlation estimates derived from the 10000 bootstrapped samples.

Appendix M



Scatterplot matrix demonstrating relations between five bootstrapped estimators of population correlations (the Pearson correlation, percentage bend correlation [PB], Winsorized correlation [WIN]) for orienting and the superior parietal cortex volume in the normal controls. Histograms represent distributions of five correlation estimates derived from the 10000 bootstrapped samples.

Appendix N



Bubble plots demonstrating relations between multivariate kurtosis and estimates of correlation. Black bubbles represent behavior-behavior relations [BB], grey bubbles represent behavior-behavior relations [SF]. The mean of the bootstrapped estimate of Pearson correlation is plotted on the X axis, whereas the mean of the bootstrapped estimate of two robust correlations is plotted on the Y axis of four bubble plots.