Cognitive Deficits in Spina Bifida
Abstract

Spina bifida myelomeningocele (SBM) is the most common and severe type of spina bifida which is a neural tube defect (NTD). Additionally to the defect of the spinal cord most cases of SBM develop an Arnold-Chiari-II malformation, which is the main reason behind the common development of hydrocephalus. Children with SBM have a rather different cognitive profile than typically developing children. Hence, this thesis reviews the neurological impact on the cognitive profile and its relation to the social impairments found for this population. The Arnold-Chiari-II malformation is a malformation of the hindbrain which affects structures of the hindbrain, midbrain, ventricular system and subcortical gray matter. These deficits lead to impairments in the cognitive domains of executive functioning, visual-spatial working memory, intelligence, language, and learning. The consequences of these cognitive deficits are often on the social aspects of life. Two aspects affected are education and work, projecting in less academic success and a higher rate of unemployment. By clarifying the relationship between all of these aspects there is hope to improve the life of these individuals, especially on an educational basis.

**Keywords:** spina bifida myelomeningocele, Arnold-Chiari-II malformation, cognition, neuroscience, social
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Cognitive Deficits in Spina Bifida

Spina bifida is a type of neural tube defect (NTD) which affects 1 to 2 infants per 1000 births (Bassuk & Kibar, 2009). Spina bifida occurs when the neural tube does not close correctly during embryogenesis and can be of different severity (Bassuk & Kibar, 2009). One of the subtypes of spina bifida is spina bifida myelomeningocele (SBM) which is characterized by a protrusion of the spinal cord, nerve roots and cerebrospinal fluid (CSF) through the back (Northrup & Volcik, 2000). When this occurs it may force the cerebellum and midbrain down towards the brainstem causing an Arnold-Chiari-II malformation (Stevenson, 2004). Almost all cases of SBM is affected by this malformation and it is only to be found when SBM is present (Stevenson, 2004; Vinck, Maassen, Mullaart, & Rotteveel, 2006). Arnold-Chiari-II malformation is a congenital malformation of the hindbrain affecting structures such as cerebellum as well as several midbrain structures and subcortical gray matter (Stevenson, 2004; Ware et al., 2014). Many children with SBM develop hydrocephalus as a consequence of the malformation (Northrup & Volcik, 2000; Stevenson, 2004). All of this together creates a rather different cognitive profile, which in turn affects the social life of these individuals (Holmbeck et al., 2003; Rose & Holmbeck, 2007; van Mechelen, Verhoef, van Asbeck, & Post, 2008).

While many studies and reviews on spina bifida do not differentiate clearly between the subtypes of this condition, the focus in this paper will be on SBM. The reasons behind focusing on SBM is that it is the most common and most severe subtype of spina bifida (Northrup & Volcik, 2000). The severity lies in the higher level lesion and the neurological impact which is not found in other subtypes (Verhoef et al., 2006).

The aim of this paper is to highlight the cognitive deficits and social impairments of SBM. This aim will be approached by describing the neurological underpinnings of SBM as well
as going through the cognitive deficits of executive functions, learning, language and intelligence and presenting the findings regarding the social impairments of this population.

Firstly a theoretical background will be presented about the different types of spina bifida and the possible causes of the defect. After this, findings regarding the neurological basis of SBM will be presented as well as theories and findings concerning Arnold-Chiari-II malformation. Then the cognitive profile in SBM, divided in several domains will be presented, followed by findings of the social impairment presented in the literature. In the discussion, the link between all aspects of spina bifida will be discussed, key findings concluded, limitations of these findings presented and future direction and implications of these findings will be discussed.

**Theoretical Background**

Spina bifida is a form of neural tube defect (NTD) in which the neural tube does not close correctly or not at all during embryogenesis, which occurs early during pregnancy. This defect can occur at different levels of the neural tube resulting in different defects (Bassuk & Kibar, 2009). If the neural tube closure is affected at the lower parts, spina bifida can emerge. NTDs can be open or close which, as the name suggests, mean that the defect is either covered by skin or the nervous tissues are exposed (Bassuk & Kibar, 2009). NTDs are the most common structural malformations of the central nervous system in human beings and, as mentioned, affect 1 to 2 infants per 1000 births (Bassuk & Kibar, 2009). The open NTD’s are the most common and include SBM (Bassuk & Kibar, 2009). 15% to 20% of NTD’s are covered with skin which is the case for meningocele (Northrup & Volcik, 2000). As briefly mentioned earlier, spina bifida comes in several types which vary in severity. The types are normally divided into two main groups; spina bifida occulta (SBO) and spina bifida cystica (SBC); Northrup & Volcik, 2000).
Spina Bifida Occulta

The mildest form of spina bifida is SBO. The word “occulta” means hidden which is a good description of the defect. In SBO, the spinal cord and meninges is within the vertebral canal but it results from a gap in at least one vertebral arch. This might manifest in a small cavity between two neighboring vertebrae, indicating that the vertebrae have not been fused together properly. This might show as a birthmark or a small dimple of hair on the patient’s lower back. When there are only one vertebra that have failed to fuse together and the spinal cord and nerves are normal, neurological symptoms are normally absent and the patient have no clinical symptoms. If more than one vertebra is involved patients might develop bowel, bladder or motor problems (Northrup & Volcik, 2000). However, in approximately 10% of otherwise healthy people, SBO occur in the lower lumbar or sacral vertebrae and is thus regarded as a normal variation in the population (Northrup & Volcik, 2000).

Spina Bifida Cystica

SBC are the umbrella term for spina bifida when a defect in the vertebral arch causes a cyst like sac on the back. This sac is filled with cerebrospinal fluid (CSF) and the spinal cord, meninges, and spinal nerves may protrude out into the sac. One type of SBC is meningocele which is a closed NTD. In the case of meningocele the spinal cord and spinal root are in their normal position but there is a sac at the location of the defect on the vertebral arch containing cerebrospinal fluid and meninges. Despite that the spinal cord is at its normal location there can be spinal cord abnormalities due to this malformation (Northrup & Volcik, 2000).

A more common and severe type of SBC is characterized further by a protrusion of the spinal cord and/or nerve roots through the vertebral arch defect into the sac. This is referred to as myelomeningocele or meningomyelocele which is an open NTD. Only 1% of children born with an open NTD are free of handicap (Northrup & Volcik, 2000). The interruption of the spinal cord
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in myelomeningocele generally causes anesthesia of the skin and paralysis of the legs, incontinence of urine and feces, and abnormalities in the hips, feet and knees, all depending on the level of the lesion on the spinal cord. The level of the lesion may also be an indicator for the degree of abnormalities in the brain as well as neurobehavioral outcomes (Fletcher et al., 2005).

When a child is born with myelomeningocele it will need multiple surgeries and invasive procedures. The first surgery is needed within 24 to 48 hours after birth in order to close the opening in the back to reduce the risk of infection, only 20% of infants who don’t get the surgery will survive to the age of two years. Approximately 80% of children born with myelomeningocele, have a presence of hydrocephalus at birth, probably caused by an Arnold-Chiari type II malformation, but not exclusively (Northrup & Volcik, 2000). The prevalence for hydrocephalus is greater for higher level lesions (Verhoef et al., 2006).

What are the causes?

There are several theories about the origins of NTD’s and Spina bifida, ranging from tea consumption (Yazdy, Tinker, Mitchell, Demmer, & Werler, 2012) to folic acid levels (Wald, Law, Morris, & Wald, 2001), and genetic components (Detrait et al., 2005). The recurrence risk for siblings of patients with NTDs without other syndromes are 2% to 5%, suggesting a genetic component (Detrait et al., 2005). In a group of families there was a history of NTDs in 8.5% of the cases. Although parent-child pairs are rare, pairs related at second or third degree are the most affected, suggesting that a small number of genes are involved (Detrait et al., 2005). One big question to account for when discussing recurrence rates within families with NTDs is whether the different levels of NTDs, which represent different defects, remain constant within the affected family. This would imply that a family can be affected with a lower NTD like spina bifida, and not inherit various versions of NTDs (Detrait et al., 2005). NTD inheritance tends to be exactly that, constant, although 30 to 40% of recurrences include an NTD phenotype, meaning
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an NTD at a different level and another defect. The theories for the reasons behind this occurrence are many, including: if it is one common underlying gene, or in families with different phenotypic presentations it may be due to several different underlying genes (Detrait et al., 2005). It might be due to timing on key environmental exposures, or could it even be the result of random chance (Detrait et al., 2005). Furthermore, NTDs are often associated with various chromosome rearrangements, such as trisomy 13 and 18, which refers to a triple set of chromosomes 13 and 18 instead of the normal two (Detrait et al., 2005). In 5 to 17% of cases with NTDs, chromosome abnormalities are found, especially aneuploidy (any variation in the number of chromosomes that involves individual chromosomes rather than entire sets of chromosomes; Detrait et al., 2005).

Folic acid is known to reduce the prevalence of NTD pregnancies if folic acid consumption is raised around the time of conception, thus raising the serum folate concentration in the blood (Wald et al., 2001). In 1992 the U.S Public Health Service (USPHS) started a program to increase folic acid consumption by improving dietary habits, fortifying foods with folic acid, and recommending all women capable of becoming pregnant to consume 0.4 mg folic acid per day. All in an attempt to decline the number of NTD affected pregnancies in the U.S (Service & States, 2004). The number of NTD affected pregnancies in the US were about 4000 (2490 cases of spina bifida specifically) in the period 1995 to 1996, and about 3000 (1640 cases of spina bifida specifically) in the period 1999 to 2000 (Service & States, 2004). This decline of about 27% highlights the partial success of the U.S folic acid fortification program (Service & States, 2004). Wald et al (2001) found that a dosage of 0.2 mg/day reduces the risk for NTDs by about 20%, 0.4mg/day, 36%, 1mg/day, 57%, 5mg/day, 85% (Wald et al., 2001). With regard to these findings it would be reasonable to suggest that the recommended dose of folic acid supplements should be 5mg/day instead of about 0.2mg/day, that is the level of the U.S folic acid
fortification and the recommendations in the United Kingdom (0.24mg) today (Wald et al., 2001). However, blood folate concentration varies from person to person, meaning that the intake of folic acid depends on the initial serum folate concentration the woman have. Women with higher initial levels may get a lower effect of the same dose of folic acid than women with a lower initial levels, meaning that the risk reduction for a dosage of 0.4mg/day can range from 23% to 52% depending on initial levels of serum folate concentration (Wald et al., 2001).

Another nutrient that may be essential for neural tube closure is vitamin B$_{12}$. Suarez, Hendricks, Felkner, and Gunter (2003) studied 343 Mexican-American women of which 157 case-women who have had NTD affected pregnancies and 186 controls with normal pregnancies. 5-6 weeks postpartum the women were interviewed and blood samples were taken. They collected data of dietary intake of b$_{12}$ and serum b$_{12}$ levels and measured and controlled for age, years of education, body mass index (BMI), dietary intake of folate, multivitamin intake, and serum folate levels. They found that women with the lowest vitamin B$_{12}$ levels showed a strong risk effect for having a NTD birth, about three times higher than the risk for women with the highest vitamin B$_{12}$ levels.

Among other theories about the cause of NTDs, diabetes and glucose levels constitute one theory. This has been shown in several mouse models where elevated glucose levels, associated with diabetes, can be a factor for NTDs (Fine, Horal, Chang, Fortin, & Loeken, 1999; Hiramatsu et al., 2002). Another may be the body mass index (BMI) of the mother since obese women, with a BMI over 29, seems to have almost twice the risk of having a child with a NTD (Rasmussen, Chu, Kim, Schmid, & Lau, 2008; Shaw, Todoroff, Schaffer, & Selvin, 2000; Watkins, Rasmussen, Honein, Botto, & Moore, 2003). Regarding tea consumption, the theory was developed from the notion that catechin (an antioxidant found in tea) reduces the uptake of folate.
However, tea consumption does not seem to be associated with a higher risk for a spina bifida affected pregnancy (Yazdy et al., 2012).

**Neurological implications and Arnold-Chiari-II malformation**

Alongside the physical disabilities mentioned before, several studies have shown that children with SBM often suffer from several cognitive disabilities. The brain abnormalities regarding SBM are varied and several factors have an impact on the cognitive profile of these children. Almost all of the cases of SBM are affected by an Arnold-Chiari-II malformation (Vinck, Maassen, Mullaart, & Rotteveel, 2006), and thus are the primary source of the brain abnormalities found in children with SBM. Arnold-Chiari-II malformation is a unique hindbrain herniation (i.e., misplacement due to pressure) which only occurs in the presence of SBM (Stevenson, 2004). This malformation is also the main reason behind the origin of hydrocephalus in these patients. The degree of anatomical disturbance, due to Arnold-Chiari-II malformation, is varied from child to child (Stevenson, 2004).

The theory that most efficiently explain the development of Arnold-Chiari-II malformation is a unified theory by McLone and Knepper (1989). This theory combines features from several other theories that do not manage to explain the origin of the malformation thoroughly. This theory points out that ventricular distension (i.e., a dilation of the ventricles) is crucial for both neural development and development of the skull. In SBM the open neural tube defect as well as incomplete spinal occlusion makes cerebrospinal fluid (CSF) drain through the central canal, thus it is not maintained in the ventricular system. Without this ventricular distention the posterior fossa never fully develops. Alongside with growth of the hindbrain this forces the cerebellum both cephalad and caudad along with the brainstem. This lack of ventricular distention produce several other anomalies and malformations such as polygyria (malformation characterized by an excessive number of small gyri), enlargement of massa
intermedia (seemingly functionless mass of grey matter in the midline of the third ventricle), and base of skull anomalies (Stevenson, 2004). It was earlier believed that the hydrocephalus associated with SBM was the cause of the Arnold-Chiari-II malformation. This is not the case since prenatal imaging has shown the development of Arnold-Chiari-II malformation before any signs of hydrocephalus. Additionally, 10-15% of children with SBM with Arnold-Chiari-II malformation do not develop hydrocephalus (Rekate, 1984). McLone and Knepper (1989) explain that the development of hydrocephalus may be due to an impaction of posterior fossa brain matter on the foramen magnum. This blocks or impairs the outflow of CSF at the foramen of Luchka and Magendie which are openings in the fourth ventricle, resulting in progressive ventriculomegaly, a brain condition occurring when the lateral ventricles become dilated.

Arnold-Chiari-II malformation makes the cerebellar vermis invariably displaced below the foramen magnum. It takes the appearance of a “peg” and can be placed really low. The cerebellum is abnormally located and as a whole it is small and seems thin. The gyri of the cerebellum are small and numerous, called polygyria. The posterior fossa is smaller as well which makes it seem crowded even though the cerebellum is smaller (Stevenson, 2004). Furthermore, abnormalities in cortical thickness, white matter integrity (Ware et al., 2014), as well as multiple ventricular anomalies are found in these patients (Stevenson, 2004). The fourth ventricle is frequently displaced and the third ventricle may take on a different shape, commonly referred to as “shark tooth deformity”. The lateral ventricle varies in appearance from nearly normal to severely deformed and the occipital horns are unduly enlarged (Stevenson, 2004). About one-third of these patients has partial or total absence of the corpus callosum which is referred to as agenesis of the corpus callosum. Untreated symptomatic Arnold-Chiari-II malformation is the leading cause of death in children with SBM under the age of two years (Stevenson, 2004).
Ware and colleagues (2014) studied gray matter volume in subcortical structures in children with SBM by using anatomical and diffusion magnetic resonance imaging (MRI). The structures examined were basal ganglia structures (caudate, pallidum, putamen), hippocampus, amygdala, and thalamus. They found a significant reduction of volume of the hippocampus as well as a significant enlargement of the putamen. Additionally they studied the mean diffusivity (MD) and the fractional anisotropy (FA) in these subcortical structures. Both of these are measured by diffusion magnetic resonance imaging (dMRI) which makes it possible to identify the diffusion process of molecules (e.g., water). MD is the measure of the total diffusion within a voxel. FA is a value that describes the degree of anisotropy (i.e., water molecules being directed in a matter that is predetermined by the tissue structure) of a diffusion process. Overall, the MD values were higher for SBM group compared to controls with exceptions for the putamen which had lower MD values and, amygdala and pallidum which had similar MD values to the controls. Regarding FA values they were overall higher for the SBM group than for controls with exception for the hippocampus (Ware et al., 2014). The mechanical effects of hydrocephalus may answer to the increased MD and FA values which in turn suggests lower density and cellular degeneration of these structures (Ware et al., 2014).

It is common in children with SBM to have abnormalities in the midbrain tectum (Williams et al., 2013). The superior colliculus is a part of the midbrain tectum and consists of two layers: the superficial layer and the intermediate layer. The superficial layer receives direct input from primary sensory regions and its outputs projects to visuomotor and motor neurons located in the more inferior intermediate layer which converge and integrates the information (Merker, 2007). The midbrain tectum is considered to be critical to spatial attention since it is a component of the posterior attentional network (Dennis et al., 2005). The Arnold-Chiari-II malformation can cause a fusion of the colliculi which forms a single mass called tectal beaking.
Cognitive deficits in spina bifida (Stevenson, 2004). Tectal beaking is associated with indices of white matter integrity of both frontal and parietal tectocortical pathways in these children compared to typically developing peers as well as other children with SBM that do not have this tectal beaking (Williams et al., 2013). These findings suggest a change in the tectocortical pathways which are not due to the mechanical effects of hydrocephalus (Williams et al., 2013). Furthermore, children with SBM display a significant decrease of tectal volume compared to typically developing controls regardless of the presence of tectal beaking (Williams et al., 2013). Decreased FA values in the posterior but not anterior tectocortical white matter pathways suggests damage to the posterior pathways, probably caused by hydrocephalus, but relatively intact anterior pathways (Williams et al., 2013). Limbic fiber abnormalities found in children with SBM and Arnold-Chiari-II malformation may account for deficits in learning and memory functions (Vachha, Adams, & Rollins, 2006).

Other variables that may contribute to the brain abnormalities are the insertion of a shunt as a treatment for the hydrocephalus, complications of the shunt, and epilepsy and its treatment (Ramsundhar & Donald, 2014). The most common reason behind shunt revisions is a blockage of the shunt, this blockage may lead to raised intracranial pressure (Hunt, Oakeshott, & Kerry, 1999). Insertion of a shunt, as well as revision of the shunt, seems to be indicators of several achievements at adult age (Hunt, Oakeshott, & Kerry, 1999). Achievement is specified by Hunt and colleagues (1999) as independent living, driving a car, and having a job. In a group of patients with spina bifida who have had a shunt inserted but no revisions after the insertion, 68% were classified as achievers. In another group of patients with spina bifida who have had a shunt inserted and shunt revisions only 28% were classified as achievers. Only 18% of patients who had have shunt revisions after the age of two were classified as achievers (Hunt et al., 1999).
Cognitive profile

This section will discuss several aspects of the cognitive profile in children with spina bifida, which have been frequently studied. Abnormal development of subcortical gray matter may account for disruptions in higher order cognition for children with SBM (Ware et al., 2014). For instance, abnormalities in thalamus and certain basal ganglia nuclei (particularly the caudate and putamen) are shown to be involved in working memory and attentional control, domains that are impaired in SBM children which will be clarified subsequently (Baier et al., 2010; Burmeister et al., 2005; Mammarella, Cornoldi, & Donadello, 2003; Rose & Holmbeck, 2007; Vachha et al., 2006; Vachha & Adams, 2005; Wiedenbauer & Jansen-Osmann, 2006).

It is important to study the cognitive deficits these children have since they are many and varied and may affect the life of these children further regarding education and employment (van Mechelen et al., 2008). The unemployment rate for young adults (16-25 years of age) with spina bifida of 53% is far higher than the 8% in the general population (15-24 years of age) in the Netherlands, and is especially low for individuals with spina bifida cystica with a higher level lesion and hydrocephalus (Barf et al., 2009). The same study found a relationship between the same variables and educational level (Barf et al., 2009). Educational level might be affected by cognitive impairments that seem to project to disabilities with math (Barnes et al., 2006; Dennis & Barnes, 2002; Mayes & Calhoun, 2006) as well as difficulties in some areas of language (Fletcher, Barnes, & Dennis, 2002). Van Mechelen and colleagues (2008) stress the importance of educational support for these children since level of education was the only significant predictor of work participation in general for this population in their study. Furthermore, impairment in executive functions such as planning, problem solving and attention as well as impairment in navigation might contribute to educational, job-related, social, and personal restriction (Burmeister et al., 2005; Dennis et al., 2005; Rose & Holmbeck, 2007; Snow, 1999;
Wiedenbauer & Jansen-Osmann, 2006). Therefore, knowledge about the cognitive profile in children with spina bifida is crucial.

**Visual-Spatial deficits**

The visuospatial working memory is a temporary store within the general working memory system proposed by Baddeley and Hitch (1974) which has the role of processing and maintenance of visuospatial information from sensory perception or from long term storage. Spatial knowledge can be divided into three domains: landmark knowledge (i.e., the knowledge of certain objects in the environment), route knowledge (i.e., knowledge of routes between these objects), and survey knowledge (i.e., overviewing representations which entail spatial relations and metric information; Wiedenbauer & Jansen-Osmann, 2006). The meaning of landmarks is twofold and refers to either landmarks as reference locus that decide the localization of other loci in the environment, or landmarks as perceived and remembered visual objects (Wiedenbauer & Jansen-Osmann, 2006). Furthermore, perception models propose two different kinds of spatial relations between objects and observers: categorical perception and coordinate perception. Categorical perception specifies spatial relationships of visual primitives that may be described by categories, feature groupings and/or verbal locatives. Coordinate perception specify how things relate to each other in space (e.g., the line and the dot are 3 cm apart). Whereas children with SBM do not seem to have problems with categorical perception, they seem to have an impaired coordinate perception (Dennis & Barnes, 2011). Although children with spina bifida (shunted for hydrocephalus) managed to point out fewer (but not significantly fewer) landmarks on the correct location in a study by Wiedenbauer and Jansen-Osmann (2006), these children do not have substantial deficits in their landmark knowledge. However, they seem to have severely limited route knowledge compared to healthy peers (Wiedenbauer & Jansen-Osmann, 2006). When matching participants for age, gender, verbal- and performance IQ children with spina
bifida needed more trials in a virtual maze before reaching the learning criterion as they made more incorrect turns and errors compared to controls. These findings indicate that an environment with more landmarks is crucial for the navigation of these individuals (Wiedenbauer & Jansen-Osmann, 2006).

Mammarella and colleagues (2003) showed that visuospatial working memory can be divided into an active and a passive component. The active component involves a greater active storage and processing of information, used when you, for example, have to actively remember both the sequential order and the visual representation of a visual stimuli. The passive component, however, is based on a passive manipulation of information used when you mainly need to sustain the recognition of the visual stimuli. Their study showed that children with spina bifida (shunted for hydrocephalus) were as good as controls in tasks that required an active component of visuospatial working memory but failed in tasks that required passive, and especially visual, functions of the visuospatial working memory (Mammarella et al., 2003).

**Executive deficits**

Executive functions are a set of high-level cognitive processes such as attention, planning, self-regulation, and goal-directed behavior. Several studies have found that children or adolescents with spina bifida have impaired executive functioning (Riddle, Morton, Sampson, Vachha, & Adams, 2005; Rose & Holmbeck, 2007; Snow, 1999), especially regarding planning, problem solving, mental flexibility (Snow, 1999), and attention (Rose & Holmbeck, 2007). One way of measuring executive function is by using the Behavior Rating Inventory of Executive Function (BRIEF; Gioia & Isquith, 2011), which is a parent and teacher rating scale that measures executive functions as displayed in the child’s everyday environment. The BRIEF scale is divided into nine domains: initiate, sustain, inhibit, shift, organize, plan, self-monitor, working-memory and emotional control. Burmeister and colleagues (2005) found that children with SBM
were rated with greater difficulties on all the BRIEF scale measures compared to healthy controls.

Rose and Holmbeck (2007) found a significant impairment of the domains initiate (i.e., the ability to initiate an activity and produce problem solving strategies or ideas independently), and working-memory, but were using a sample with varying types of spina bifida although the majority (71%) was shunted for hydrocephalus. However, the varying types of spina bifida in this sample gives an indication that the effects of hydrocephalus (and/or shunt surgery) may be a major factor for the cognitive disabilities found. Within the spina bifida sample, shunt status (whether or not a participant have required shunting for hydrocephalus) was a significant predictor of both the Cognitive Assessment System (CAS; Naglieri & Das, 1997) and BRIEF performance (Rose & Holmbeck, 2007).

This study by Rose and Holmbeck (2007) found impairments regarding planning on one of the test used. Children with spina bifida were impaired on the planning sub-tests of the performance-based CAS but did not show any impairments on the BRIEF questionnaire (which is answered by parents and teachers). The two tests measure different types of planning. CAS measure the ability to develop and rapidly execute problem solving strategies, whereas BRIEF measures the social and behavioral manifestations of planning ability. The difference between the outcomes of these two tests may be an indication for the type of planning which is impaired. Meaning that children with spina bifida may have an reduced ability with rapid and efficient development of problem solving strategies but do not have difficulties in their ability to plan for and anticipate consequences in their daily activities (Rose & Holmbeck, 2007).

Regarding attention, children with spina bifida do not seem to have impaired sustained attention (i.e., the ability to maintain a consistent behavioral response and to detect unpredictably occurring signals over a long period of time), but are impaired when it comes to focused attention...
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(i.e., the ability to respond separately to a specific stimuli; Rose & Holmbeck, 2007). However, the results might be affected by the use of two different types of tests for sustain and focused attention in this study. Sustain attention were measured using the parent/teacher BRIEF questionnaire, whereas focused attention were measured by the performance-based CAS (Rose & Holmbeck, 2007).

In orientation of attention we can either shift attention by overt movements of the head, body or eyes, or covert, meaning a shift of attention without moving our head, body or eyes. Furthermore overt orientation of attention can be automatic, as in orienting towards salient information, and can be tested using exogenous cues, or effortful, as in voluntary shifts of attention towards something we find interesting and can be tested by using endogenous cues (Dennis et al., 2005). Children with SBM seem to have a slowed covert orientation, compared to matched controls, on both exogenous and endogenous cues that concern attention disengagement (Dennis et al., 2005). This may be due to the dysmorphology (i.e., abnormal development of tissue form) of the midbrain and thinning of the posterior cortex that these children display due to Arnold-Chiari-II malformation, regions that are associated with the control of covert orienting (Dennis et al., 2005). Furthermore, among children with SBM the prevalence rate for Attention Deficit Hyperactive Disorder (ADHD), based on parent rating scales, is higher (31%) than for the general child population (5%) as presented in the Diagnostic and Statistical Manual of Mental Disorder, fifth edition (DSM-V; Burmeister et al., 2005; American Psychiatric Association, 2013). The parent rating scales used by Burmeister and colleagues (2005) were based on the DSM-V criteria. The group of children with SBM and ADHD did not differ in number of shunt revisions compared with the group of children with SBM, without ADHD (Burmeister et al., 2005).
Learning deficits

Mayes and Calhoun (2006) studied the frequency of learning disabilities in children with clinical disorders among which one of the groups were children with spina bifida. They found that 60% of the children in the spina bifida group (with normal intelligence i.e. IQ > 80; mean IQ: 89) had learning disabilities and mainly disabilities with math and written expression (i.e., the ability to express oneself in writing). 33% of the spina bifida group had learning disabilities in math, and 40% had learning disabilities in written expression. The two other learning disabilities studied; reading and spelling, did not seem to be disabled in this group.

Regarding math and numeracy young adults with SBM seem to have poorer computation accuracy (which was related to the working memory of numbers), computation speed, problem solving, and functional numeracy than expected for their age and those skills are furthermore poorer than their own level of reading decoding (Dennis & Barnes, 2002). The compromised functional numeracy was related to the number of lifetime shunt revisions (Dennis & Barnes, 2002). For these individuals it seems that poor math problem solving skills in their childhood may translate into poor problem solving and numeracy further on in adulthood (Dennis & Barnes, 2002). These difficulties are likely to limit the academic achievement, vocational success and functional independence for individuals with SBM (Dennis & Barnes, 2002). Overall children with this condition have less mastery of math facts (basic facts in addition, subtraction, multiplication, and addition, i.e., 3+3=6; Barnes et al., 2006). Many have hypothesized a link between deficits in visual-spatial working memory, visual memory, and visual-spatial functioning, and disabilities in mathematics (McLean & Hitch, 1999; Rourke, 1993; Share, Moffitt, & Silva, 1988). Barnes and colleagues (2006) did not find this link and furthermore found that visual-spatial errors in multi-digit arithmetic were not elevated in children with SBM.
Furthermore, these children seem to have problems with remembering a long list of words, due to impairment in memory span (Vachha & Adams, 2005). In a memory task they had to remember a long list of words, some words (fruits) were of higher value than other words (animals). Children with SBM remembered significantly fewer words than controls. This study also suggests that children with SBM are impaired in their ability to use the most efficient strategy in learning items of different value in order to achieve a higher score. The majority, 65%, of the SBM group reported that they tried to remember all the words, whereas 85% of controls reported that they tried to remember the items with the higher value (Vachha & Adams, 2005). The ability to remember information of relevance among less relevant information is an important skill for success in school, something that children with SBM seem to have problems with (Vachha & Adams, 2005). Children with SBM seem to reach poorer educational success. One-third of the children in a study of young adults with spina bifida had need for special education or had not reached education beyond primary school and only 16% of the sample had higher level education (Barf et al., 2009). They also found a link between lower education and having spina bifida cystica, a higher level lesion and the occurrence of hydrocephalus (Barf et al., 2009).

Language deficits

Regarding language most children with SBM have a good vocabulary (Horn, Lorch, & Culatta, 1985) and comprehension of grammar seem to improve more with age (for children with hydrocephalus) compared to healthy controls (Dennis, Hendrick, Hoffman, & Humphreys, 1987). However they seem to have difficulties in other areas of language (Fletcher et al., 2002). Their difficulties are mainly in construction of meaning and in pragmatic communication (social communication).
Many children with SBM (who are in the intellectually average range) show the core feature of the “cocktail party syndrome” which produces a language that lacks content and essence, and fails to deliver the central information of a subject. Thus, their language tends to be verbose and complicated (Dennis, Jacennik, & Barnes, 1994). The term “cocktail party syndrome” is described by Tew (1979) in five steps: (1) preservation of response, with repetition of an earlier statement made by the child, (2) Excessive use of social phrases in conversation, (3) An over-familiarity in manner, not normally expected in a child, (4) Introduction of personal experience into the conversation, usually in an irrelevant and inappropriate context, and (5) Fluent and well-articulated speech. Thus, the “cocktail party syndrome” is used to describe language that within a conversation is contextually aimless, irrelevant and inappropriate, despite that it is articulate and coherently expressive (Tew, 1979). However to describe these differences in language as a syndrome might be misleading (Dennis et al., 1994).

Construction of meaning and in pragmatic communication require flexible language processing in real time which seems to be impaired due to brain abnormalities caused by the Arnold-Chiari-II malformation (Fletcher et al., 2002)

**Intelligence**

It has been commonly reported that hydrocephalic children are more impaired on performance IQ than verbal IQ (Berker, Goldstein, Lorber, Priestley, & Smith, 1992; Dennis et al., 1981; Donders, Rourke, & Canady, 1991; Fletcher et al., 1992). Similar results have been found when comparing children with SBM and children with spina bifida without cerebral malformations (Vinck et al., 2010). In this study by Vinck and colleagues (2010) they used the Wechsler Intelligence Scale for Children – III (WISC-III; Wechsler, 1991) which was administered to measure general intelligence in children aged 6-16 years of age. The WISC-III are divided into verbal IQ (VIQ), performance IQ (PIQ), and full scale IQ (FSIQ). Although
scores on VIQ were similar (SBM: 94, spina bifida: 98), scores on PIQ (SBM: 77 spina bifida: 98) and FSIQ (SBM: 85, spina bifida: 100) differed significantly (Vinck et al., 2010). However, when comparing children with SBM with healthy controls Jacobs, Northam, and Anderson (2001) found that children with SBM performed significantly poorer on all intelligence tests in the WISC-III including VIQ (SBM: 84,5, controls: 105,7), PIQ (SMB: 79,3, controls: 106,8), and FSIQ (SMB: 80,8, controls: 106,7; Jacobs et al., 2001). In an older test on intelligence among these children (Tew, 1977) using an older version of the WISC, similar scores were presented. Barf and colleagues (2003) studied the cognitive status of young adults (16-25 years of age) with spina bifida cystica either with or without hydrocephalus and used the Standard progressive matrices (Raven, 1996) to measure general intelligence (mean IQ is 100). A group mean of 83 for the hydrocephalus group and 93 for the group without hydrocephalus was presented and one fifth on the hydrocephalic group had an IQ under 70 (Barf et al., 2003). In addition to general intelligence, memory, verbal learning, executive function and reaction time was tested, and IQ significantly correlated with all but one of the other cognitive scores (Barf et al., 2003).

Holler, Fennell, Crosson, Boggs and Mickle (1995) as well as Barf and colleagues (2003) present that malformation of the corpus callosum appear to be negatively related to intelligence, whereas Ralph, Moylan, Canady, Simmons (2000) contradicting finding suggested that the number of shunt revisions was a possible answer to why some children with SBM may have a lower IQ, which goes in line with the findings of Barf and colleagues (2003). Both studies found that five or more shunt revisions had a negative effect on IQ (Ralph et al., 2000; Barf et al., 2003). Furthermore, there may be a relationship between impaired performance IQ and performance in the attention and executive domain (Riddle et al., 2005).
Whereas mean intelligence is generally known to be set at 100, the mean scores of children with SBM is generally lower and seems to be due to cerebral malformation including hydrocephalus (Barf et al., 2003; Jacobs et al., 2001; Tew, 1977; Vinck et al., 2010).

Social impairments

Children with spina bifida (age 8-9) exhibit lower levels of psychosocial adjustment compared with healthy peers (Holmbeck et al., 2003). They seem to be more socially immature and are more dependent on adults for direction and guidance. They are less likely to initiate social contact and to make independent decisions. Furthermore, they seem more passive and less engaged when observed during family interaction (Holmbeck et al., 2003). As a result of this, children with spina bifida tend to have fewer social contacts outside of school compared to healthy peers (Holmbeck et al., 2003). These impairments may be linked to their deficit regarding pragmatic communication mentioned before (Fletcher et al., 2002; Holmbeck et al., 2003). Furthermore, the deficits in attention and executive function found in children with spina bifida have been found to be predictive of these social adjustment difficulties (Rose & Holmbeck, 2007). Holmbeck and colleagues (2003) hypothesize that the social difficulties experienced in childhood may make them more likely to experience depressive affect during adolescence. Adolescents with spina bifida have been found to be at greater risk for having depressive symptoms such as depressive mood, low self-worth, and suicidal ideation compared to able-bodied peers (Appleton et al., 1997).

When asking adolescents (12-21 years of age) about the future they reported that they felt less positive about being able to go out on dates, being treated the same as other kids, and job opportunities (Sawin, Brei, Buran, & Fastenau, 2002). As mentioned before, employment seems to be a major issue for individuals with spina bifida, with only 47% of 92 participants who had
finished their education having a regular job (Barf et al., 2009). In other another sample (of 179 participants), 62.5% worked at least for one hour per week, of which 22.4% worked in a sheltered workplace. Sex, educational level, and self-care independence were significant predictors of full time employment, and for paid work only level of education was a significant predictor. When trying to find work, the most common problem reported (stated by 57% of the sample) was an unwilling attitude among the employees (van Mechelen et al., 2008). Furthermore, lower scores on VIQ, PIQ, and functional math skills have been found to be associated with unemployed status. For hydrocephalic children with spina bifida there seems to be significantly more problems when it comes to out of school activities compared to children with spina bifida without hydrocephalus (Cate, Kennedy, & Stevenson, 2002).

Whereas intelligence, memory, and word production do not seem to be related to subjective quality of life (SQoL) in young adults with spina bifida and hydrocephalus, executive function seems to be (Barf, Post, Verhoef, Gooskens, & Prevo, 2010). Scores on executive functioning was a stronger determinant of SQoL than functional independence in a study by Barf and colleagues (2010). The authors of this particular study suggests that the reason behind why executive functioning is related to SQoL might be due to a more direct or more substantial impact of executive function on daily activities as they interfere with more complicated or more articulated activities. This indicates that disadvantages in planning, mental flexibility or attention can affect independent functioning, especially in new situations, for children with hydrocephalic spina bifida (Barf et al., 2010). Hetherington, Dennis, Barnes, Drake and Gentili (2006) found a relationship between functional math skills and overall quality of life.

When studying resilience in adults with spina bifida, Hayter and Dorstyn (2013) found a significant positive correlation between resilience, self-esteem, and self-compassion as well as an significant negative correlation between resilience and depression, anxiety, and stress.
Furthermore, this psychological distress was associated with lower levels of self-esteem and self-compassion. The authors suggest that the cumulative medical stressors that are experienced by individuals with spina bifida (in addition to physical disability) have a negative impact on psychological functioning (Hayter & Dorstyn, 2013). Lastly, although a minority, it is important to highlight that more than one-fifth of a sample of 97 adults with spina bifida had experienced social isolation and bullying as a consequence of their disability (Hayter & Dorstyn, 2013).

Discussion

Spina bifida is a lower level NTD which comes in different variations at different levels of severity (Bassuk & Kibar, 2009; Northrup & Volcik, 2000). SMB is the most severe type of spina bifida which often is accompanied by neurological deficits such as Arnold-Chiari-II malformation and hydrocephalus (Stevenson, 2004). The causes behind NTD and spina bifida are not determined, and several theories and findings may yield some answers. Perhaps there is a network of aspects underlying the cause of NTD and spina bifida. Some of the components behind the cause may be genetic components (Detrait et al., 2005), folic acid levels (Wald et al., 2001), vitamin b\textsubscript{12} levels (Suarez et al., 2003), diabetes and glucose levels (Fine et al., 1999), and BMI (Watkins et al., 2003).

The aim of this paper was to highlight the cognitive deficits and social impairments of SBM. To fully understand the cognitive deficits and their social implications, the neurological basis of SBM needs to be reviewed. Several factors implement the neurological aspect of SBM. One is the occurrence of hydrocephalus, the other is the Arnold-Chiari-II malformation which also is the main cause of hydrocephalus. However, hydrocephalus can be present in this population without Arnold-Chiari-II malformation, and the Arnold-Chiari-II malformation can be present without hydrocephalus. Arnold-Chiari-II malformation primarily affects structures of the
hindbrain and midbrain. The cerebellum is severely deformed and the ventricular system of the brain affected, partly because of a blockage caused by a displacement of the cerebellum (Stevenson, 2004). Differences in the volume of gray matter may explain many of the cognitive deficits. Reduction in volume of the hippocampus as well as enlargement of the putamen (Ware et al., 2014), which are structures that are involved in learning, may give some answers regarding the disabilities in this area. Furthermore, abnormalities in limbic fibers may contribute to the learning and memory disabilities (Vachha et al., 2006). The presence of tectal beaking may be linked to deficits in covert orientation of attention, and damage to posterior tectocortical white matter pathways as well as decreased tectal volume may be a cause of attention deficits (Williams et al., 2013).

The cognitive profile for children with SMB differs between individuals, although some aspects have been suggested to correlate with the population with spina bifida. In the visual-spatial domain children with SBM or spina bifida with hydrocephalus seems to be impaired on coordinate perception, have severely limited route knowledge, and impairments on passive functions of visual-spatial working memory (Dennis & Barnes, 2011; Mammarella et al., 2003; Wiedenbauer & Jansen-Osmann, 2006). The knowledge of landmarks does not seem to be impaired in these individuals which implies that an environment with more landmarks would be beneficial for the navigation of individuals with hydrocephalic spina bifida. The findings regarding active and passive components of visual-spatial working memory seem to contradict the findings concerning landmarks. One would assume that landmarks would be a passive stimulus and route knowledge an active stimulus. However, if landmarks are sequentially memorized it could imply the use of an active component. Thus, future studies on the difference between memorization of a single landmark and sequentially presented landmarks would add clarity to this issue.
Problems regarding executive functions such as planning, problem solving, mental flexibility and attention have been found. In planning, Rose and Holmbeck (2007) presented a difference between two types of planning which were measured with two different scales. One scale measured the social and behavioral manifestation of planning ability whereas the other measured the ability to develop and rapidly execute problem solving strategies. However, this statement is problematic since one of the measures also require problem solving skills. Problem solving, by itself, has been found to be impaired in this population (Snow, 1999), for example when testing problem solving in math and on the BRIEF scale (Dennis & Barnes, 2002; Rose & Holmbeck, 2007). Children with hydrocephalic spina bifida have an impaired ability to respond separately to a specific stimulus which is called focused attention (Rose & Holmbeck, 2007). However, they do not seem to be impaired when it comes to the ability to maintain attention. This later finding needs to be addressed further since it was found by using a questionnaire answered by parents and teachers of the child and were thus not measured by actually testing the child’s ability of sustained attention.

Concerning the learning disabilities which have been found to be present in 60% of the sample in a study by Mayes and Calhoun (2006). It is interesting to note that the mean IQ was 89 and IQ was further controlled to be over 80, meaning that the sample were divided into two groups based on having an IQ score over or under 80. The group with an IQ under 80 were not included when studying learning disabilities in this study. The rather high prevalence of 60% may be severely affected by the small sample of 23 children. Further studies should study the prevalence of learning disabilities for this group, but with a larger sample, and include all participants, and control for IQ but not exclude children with IQ under 80. Regarding IQ and intelligence, PIQ is often reported to be impaired whereas VIQ and FSIQ are in the normal range (Berker et al., 1992; Dennis et al., 1981; Donders, Rourke, & Canady, 1991; Fletcher et al., 1992;
Vinck et al., 2010). However, many of these findings are rather on hydrocephaly than on SBM per se. Conversely, studies have found impairments on all three IQ measures when studying children with SBM. This may imply that impairments on solely PIQ are associated with hydrocephalus whereas the neurological deficits of SBM may affect VIQ and FSIQ as well.

Impairments of several aspects of social life for this population have been observed. Children with spina bifida tend to have fewer contacts outside of school. This may be attributed to their lower levels of psychosocial adjustments which are manifested in that these children seem to be more socially immature, depend more on adults, do not initiate social contact as much and are less engaged in social situations compared to healthy peers (Holmbeck et al., 2003). Additionally, there might be a relationship between social difficulties in childhood and depressive symptoms in adolescence (Holmbeck et al., 2003). Higher risk for depressive symptoms has been found for adolescents with spina bifida (Appleton et al., 1997), thus making the relationship probable.

This may be due to the cognitive deficits of pragmatic (or social) language (Fletcher et al., 2002) and deficits in attention and executive functions (Rose & Holmbeck, 2007) which in turn may be attributed to deficits in tectum and white matter connectivity (Williams et al., 2013). Furthermore, a study demonstrates a relationship between SQoL and executive functioning (Barf et al., 2010). The authors provide a discussion about this relationship, suggesting that disadvantages in functions such as planning, attention or mental flexibility may affect social situations where independent functioning is crucial. This especially regards new situations where these children cannot rely on previously learned experiences (Barf et al., 2010).

The social domains of work and education seem to be severely affected by spina bifida in several ways. It can be partly due to negative attitudes towards disabled individuals that still exist in our society such as bullying, social isolation (Hayter & Dorstyn, 2013) or negative attitudes
from employers (van Mechelen et al., 2008). Relationships between level of education and prevalence of paid work have been found, indicating that educational support is important (van Mechelen et al., 2008). Unemployment seems to be associated with lower scores on VIQ, PIQ and math skill which supports the previous statement. Several cognitive deficits might affect the educational success of children with spina bifida, such as planning, problem solving, attention and learning deficits. Regarding learning these children need extra support when it comes to acquiring the basic math knowledge (Dennis & Barnes, 2002) as well as when it comes to sifting out relevant information from less relevant information (Vachha & Adams, 2005). Limbic fiber abnormalities may account for some of the learning deficits (Vachha et al., 2006). Children with SBM may as well benefit from having support with planning of their studies. Furthermore, deficits in written expression may imply a need for rethinking the way knowledge is tested in these children. However, a sufficient way in testing knowledge in this population needs to be studied. Written exams may be affected by deficits in written expression, multiple-choice may be affected by deficits in sifting out information, and oral exams may be affected by deficits in language.

Resilience seems to be negatively affected by medical stressors that come with this condition (e.g., surgeries). Psychological distress may decrease levels of self-esteem and self-compassion. However, higher levels of self-esteem and self-compassion are positively correlated with higher levels of resilience (Hayter & Dorstyn, 2013). These finding may imply a need for active work with self-esteem and self-compassion for individuals who have gone through several medical stressors. Additionally, self-esteem may affect educational and vocational success as well as social situations overall.

All findings in this thesis imply a link between SBM and the impaired social situation of these individuals by describing the neurological deficits and its impact on cognitive functions.
However, there are some limitations of the studies on spina bifida that complicates their findings. The terminology in this field is somewhat confusing with several terms for the same concept, which makes it difficult to differentiate the types of spina bifida and what deficits are caused by what. Some studies use the term spina bifida with hydrocephalus which do not differentiate children with the occurrence of Arnold-Chiari-II malformation from those without. It is known that Arnold-Chiari-II malformation is the main cause of hydrocephalus, but that there are cases of spina bifida with hydrocephalus without this malformation although it is less common. That hydrocephaly impairs cognition is known, but the effects of solely Arnold-Chiari-II malformation is still scarcely studied. Further research on this subject should try to differentiate the neurological deficits to find the specific profile for SBM. Furthermore, there are studies with samples of various forms of spina bifida where no differentiation is made. It is important to be cautious when drawing conclusions about the cognitive profile of spina bifida when some display damages to the brain and some do not.

**Conclusion**

In conclusion, children and adolescents with SBM have, as a consequence of the neural tube defect and Arnold-Chiari-II malformation, cognitive deficits that affect their social life and education. Regarding education the cognitive deficits affect school related domains such as learning. However, there are other aspects to educational success that these children need support with. These domains concern planning, sifting information, problem solving and attention. Therefore, knowledge about the whole picture of spina bifida is important to be able to provide the best educational support for these children and adolescents. By developing an educational support in the form of a mentor or coach that will meet with the child or adolescent once a week, many of these weaknesses in school might be resolved. The coach can, for example, help the
child with planning and structure of their studies as well as being a support in the school environment.
References


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