



Psychological adjustment of young subjects with Möbius sequence and their primary caregivers' strain and life satisfaction: First longitudinal data



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ARTICLE INFO

No. of reviews completed is 2

Keywords:

Moebius Syndrome
children and adolescents
psychological, adjustment
strain
life satisfaction
longitudinal data

ABSTRACT

Aims/Methods: At present, there is no information about the course of psychological adjustment in young subjects with Möbius sequence (MS) and their parents' strain and life satisfaction. To fill this gap, we performed a four-year follow-up study. Parents were anonymously asked to fill out the Child Behavior Checklist 4-18 [CBCL/ 4-18] or the Young Adult Behavior Checklist 18-30 [YABCL/ 18-30] and the Freiburger Personality Inventory-Revised [FPI-R], subscales strain and life satisfaction.

Results: 12 males and 14 females (mean: 15.20 years, standard deviation: 3.48 years) could be included in the follow-up (response rate: 83.9%). Compared to the general population, subjects with MS showed significantly higher scores on almost all CBCL scales (exception: externalizing problems) at T1 and T2. At both study times, parental strain and life satisfaction were not significantly different from findings in the general population. No significant longitudinal changes could be found for CBCL scales, parental strain and life satisfaction.

Conclusions: Problems with psychological adjustment seem to be frequent among younger subjects with MS. Therefore, careful monitoring as well as early and adequate interventions, if indicated, are crucial for subjects with MS, not only with regard to somatic complaints but also to aspects of adjustment.

What this paper adds?

This paper adds to our so far very limited knowledge on psychological adjustment among children and adolescents with MS and their primary caregivers' strain and life satisfaction over time. In this paper, we present first longitudinal data on these aspects which are very important for counselling families with a child with MS. While we found increased rates of clinically significant problems with psychological adjustment and parental strain at both study points, no statistically significant changes with time could be found. The results of this study emphasize that careful monitoring as well as early and adequate interventions, if indicated, are crucial for subjects with MS, not only with regard to somatic complaints but also to problems with psychological adjustment.

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<https://doi.org/10.1016/j.ridd.2018.11.004>

Received 15 August 2017; Received in revised form 16 September 2018; Accepted 8 November 2018

Available online 19 November 2018

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1. Introduction

Möbius syndrome or Möbius sequence (MS; Online Mendelian Inheritance in Man no. 157900), is a non-progressive congenital condition usually defined as a combination of facial weakness (uni- or bilateral) with impairment of ocular abduction (uni- or bilateral) (Briegel, 2006; Verzijl, van der Zwaag, Cruysberg, & Padberg, 2003). Recently, full vertical motility of the eyes has been suggested to be another minimal diagnostic criterion (MacKinnon et al., 2014). Estimated prevalence rates range from 0.0002 to 0.002 % of births (Briegel, 2006). Etiology and pathogenesis of the sequence are still not fully understood (Briegel, 2006).

Intellectual disability seems to occur in about 10% of children and adolescents with the sequence (Briegel, Schimek, Knapp et al., 2009; Kuklik, 2000), whereas disturbances in psychomotor and speech development have been reported to be very common (Sjögreen, Andersson-Norinder, & Jacobsson, 2001; Verzijl et al., 2003). A secured diagnosis of autism spectrum disorders (ASD) has been reported in 18 patients throughout six studies worldwide with a total of 132 Möbius patients included (Bogart, Briegel, & Cole, 2014). However, 17 of these 18 had intellectual disabilities. Moreover, in Möbius patients without intellectual disabilities a maximum ASD rate of 5.3% has been found (Briegel, Schimek, Kamp-Becker, Hofmann, & Schwab, 2009; Briegel, Schimek, & Kamp-Becker, 2010) indicating that there is primarily an association of ASD with intellectual disability and not with MS (Briegel, 2006). Just to compare, population-based studies have revealed a prevalence of ASD in subjects with intellectual disability in general of about 18%, whereas 75% of subjects with ASD have comorbid intellectual disability (Bourke, de Klerk, Smith, & Leonard, 2016; Tonnsen et al., 2016).

With regard to psychological adjustment, social problems have been repeatedly reported to be more frequent among children and adolescents with MS when compared to the general population (Briegel, Schimek et al., 2010; Briegel, 2012; Briegel, Hofmann, & Schwab, 2010; Strobel & Renner, 2016). Moreover, one cross-sectional study suggested a significant increase of social problems with age (Briegel, Hofmann et al., 2010). As facial expression is essential for communication and social interaction (Tickle-Degnen, 2006), it has been suggested, that subjects with MS are at high risk to experience rejection or lack of reinforcement when they grow older (Bogart et al., 2014; Briegel, 2006). Other features of MS like drooling of saliva, dysarthria and malformations of the extremities may further increase the risk for social rejection and lead to stigmatization (Bogart, 2015). In line with this, focus group studies have revealed experiences of teasing, bullying and social strain among subjects with MS with the teenage years being the most challenging life stage (Bogart, Tickle-Degnen, & Joffe, 2012; Bogart, 2015). These negative experiences, together with the patient's own perception of being different, might enlarge the risk of developing internalizing problems and subsequent psychiatric disorders (Briegel, 2007). However, in their self-perception, 9-15 year old subjects with MS seem to experience no elevated levels of anxiety, depression, and impulsivity (Briegel, 2012) whereas results for adult subjects are inconclusive with regard to depression and satisfaction with life (Bogart & Matsumoto, 2010; Briegel, 2007). So far, there have been no longitudinal studies on the psychological adjustment of subjects with MS although the results of such studies could be very helpful for counselling and treatment.

When compared with age and sex matched people, the primary caregivers of children and adolescents with MS have been found to experience normal life satisfaction, but increased rates of clinical strain (Briegel, Hofmann, & Schwab, 2007; Briegel, Hofmann et al., 2010). However, compared with other parents of physically and / or intellectually disabled children, they seem to experience less parental stress (Briegel et al., 2007; Briegel, Hofmann et al., 2010; Briegel, Schimek et al., 2010; Briegel, 2018). In a cross-sectional study, maternal stress was significantly positively correlated with disability-related problems, and mothers reached average levels of coping strategies like partnership intensification, ability to meet own needs and use of social support (Briegel, 2018).

To better understand how life satisfaction and strain of primary caregivers of children and adolescents with MS develop over time, and what kind of support might be needed, longitudinal studies which are missing until now are urgently needed.

2. Aims

The aim of this study was to assess aspects of psychological adjustment in young subjects with MS and their primary caregivers' strain and satisfaction with life by means of a four years follow-up of the study described by Briegel, Hofmann et al. (2010).

3. Methods

3.1. Participants

With support of the German MS foundation all primary caregivers who could have been included in the first study on psychological adjustment and parental strain and life satisfaction (T1; Briegel, Hofmann et al., 2010) were anonymously asked to participate in a four years follow-up study (T2). Inclusion criteria were congenital facial weakness (uni- or bilateral) with concomitant impairment of ocular abduction (uni- or bilateral).

By post, all caregivers received:

- a special questionnaire to compile personal, somatic and psychosocial history of the subjects with MS,
- the German version of the Child Behavior Checklist [CBCL] 4-18 (Achenbach, 1991; Arbeitsgruppe Deutsche Child Behavior Checklist, 1998) for patients up to the age of 18 years. This well standardized 113 items questionnaire for parents of children aged 4-18 years (ratings: 0 for not true, 1 for somewhat or sometimes true, and 2 for very true or often true) has been validated for the German general population. The CBCL/ 4-18 is based on statistical groupings of sets of behaviours that typically occur together, and comprises the following eight constructs or symptom scales: Social Withdrawal, Somatic Complaints, Anxiety/Depression,

Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior. The CBCL/ 4-18 also allows the examination of two broader groupings of syndromes: Internalizing Problems (which combines the Social Withdrawal, Somatic Complaints, and Anxiety/Depression scales), and Externalizing Problems (combining the Delinquent Behavior and Aggressive Behavior scales). The Total Problems score represents the sum of all the problem items. Results are given as *t*-values (mean *t*-value: 50, standard deviation: 10). For a symptom scale, clinical cases are defined as *t*-values > 70, which means that about 2% of the general population are categorized as clinical, whereas for a global scale about 8% of the general population show *t*-values in the clinical range (*t*-value > 63).

- the German version of the Young Adult Behavior Checklist [YABCL] 18-30 (Achenbach, 1997; Achenbach & Arbeitsgruppe Deutsche Child Behavior Checklist, 1998) for patients of the age of 19 years or older. The YABCL/ 18-30 is a well validated 113 items questionnaire for parents of 18-30 year old adults (ratings: 0 for not true, 1 for somewhat or sometimes true, and 2 for very true or often true). Similar to the CBCL/ 4-18, it comprises 8 symptom scales (Withdrawn; Somatic Complaints; Anxious/Depressed; Thought Problems; Attention Problems; Intrusive; Aggressive Behaviour; Delinquent Behavior) and 3 global scales (Internalizing Problems, Externalizing Problems, Total Problems). Internalizing Problems combines the two scales Withdrawn and Anxious/Depressed while Externalizing Problems comprises the three scales Intrusive, Aggressive Behaviour and Delinquent Behaviour. The Total Problems score represents the sum of all the problem items. As there are no German norms, American norms were used. Results are given as *t*-values (mean *t*-value: 50, standard deviation: 10). Clinical cases are defined analogously to the CBCL/ 4-18 (see above).
- the Freiburger Personality Inventory-Revised [FPI-R], (Fahrenberg, Hampel, & Selg, 2001), subscales strain and life satisfaction, to assess parents' experiences. The FPI-R is a well standardized and validated German personality questionnaire. Subscales strain (tense, overwrought, stressed vs. unstrained, unpressured, able to handle stress) and life satisfaction (contented with life, optimistic, hopeful vs. discontented, depressed, negative attitude towards life) comprise 12 items each (true / not true answer). Results are given as stanine values (mean: 5, standard deviation: 2). A stanine value of nine (> 95th percentile) for strain, and of one (< 5th percentile) for life satisfaction was defined as clinical.

Statistical analysis of the results was done using SPSS 24.0. Based on the rarity of MS and on the clinical importance of detecting change (if it is there), we decided to use predominantly parametric statistical methods – despite our small study sample. One reason is that parametric tests provide more options for statistical analysis, e.g. there is no equivalent non-parametric test for multivariate repeated measures analyses of variance (MANOVA) which we wanted to use to analyze changes in the main outcomes – CBCL/ 4-18 scales and the two subscales of the FPI-R. Moreover, some authors have suggested that parametric tests are quite robust (Rasch & Guiard, 2004). We also preferred parametric tests to be consistent but – where possible – additionally analyzed the data non-parametrically (e.g. Wilcoxon test). These non-parametric analyses revealed similar results.

The following parametric tests were used: the paired student *t*-test to analyze differences between T1 and T2, the one sample *t*-test to analyze differences between the study population and the general population, and the *t*-test for independent samples to analyze differences between groups. For correlations we used Pearson's *r*.

The statistical significance of changes in frequencies of clinically significant CBCL/ 4-18 global scales (Internalizing, Externalizing, Total Problems) was assessed by means of the McNemar test, a nonparametric test for changes in binary outcomes.

To analyze changes in the main outcomes – CBCL/ 4-18 scales and the two subscales of the FPI-R – we performed multivariate repeated measures analyses of variance (MANOVA). As possible influence factors of the CBCL scales, FPI baseline values were included in the model as covariates, allowing for possible interaction of time and baseline characteristics. As CBCL/ 4-18 *t*-values were used, no correction for the influence of the child's age and gender was needed. In the models for changes on FPI-R scales, age and gender were included as control variables.

Cohen's *d* (Cohen, 1988) was calculated for differences of group means ($d = M_1 - M_2 / \sigma_{\text{pooled}}$). *d* = .2, .5 and .8 correspond to small, medium and large effects.

Statistical significance was defined by $p < 0.05$ (two-tailed).

Based on the rarity of MS and on the clinical importance of detecting change (if it is there), we did not correct for type 1 error despite the relatively large number of analyses performed.

4. Results

4.1. Participants

Primary caregivers of 31 children and adolescents with MS aged 4-17 years could be included in the first study (T1; for more details see Briegel, Hofmann et al., 2010). The four years follow-up (T2) comprises 26 subjects, 12 males and 14 females (age: 8 - 21 years, mean: 15.20 years, standard deviation: 3.48 years). Six subjects were 19 years or older. In most cases, MS had been diagnosed by a geneticist or a pediatrician, median age at diagnosis was 13 weeks.

Table 1 gives a summary of the subjects' medical problems at T1 and T2 according to their primary caregivers' informations.

At T2, seven subjects had been seen by a child and adolescent psychiatrist for various reasons (one more than at T1). Only two subjects had been diagnosed with a psychiatric disorder, at T2 one of them was treated with escitalopram for depression. At T2, two subjects had psychotherapy (versus one subject at T1).

Table 2 shows the subjects' school careers at T1 and T2. After elementary school German students typically have to choose between three types of secondary schooling modalities: „Hauptschule“ (grades 5-9), which is supposed to prepare for less-skilled jobs,

Table 1
Somatic problems of subjects with MS at T1 and T2

Somatic problem:	Number of affected subjects (percent):	
	T1	T 2
Facial paralysis	26: 17 bilateral (65.4) 9 unilateral (34.6)	26: 17 bilateral (65.4) 9 unilateral (34.6)
Abducens paralysis	26: 25 bilateral (96.2) 1 unilateral (3.8)	26: 25 bilateral (96.2) 1 unilateral (3.8)
Strabism	15 (57.7)	8 (30.8)
Malformation of feet	13 (50.0)	13 (50.0)
Malformation of hands	10 (38.5)	10 (38.5)
Hearing loss	5 (19.2)	3 (11.5)
Poland sequence	4 (15.4)	5 (19.2)
Ptosis	3 (11.5)	1 (3.8)
Congenital heart defect	3 (11.5)	3 (11.5)
Arthrogryposis	3 (11.5)	4 (15.4)
Scoliosis	2 (7.7)	3 (11.5)
Pierre-Robin sequence	1 (3.8)	1 (3.8)
Seizures	1 (3.8)	2 (7.7)

Table 2
School career of subjects with MS at T1 and T2

School types attended:	Number of subjects (percent):	
	T1	T 2
Elementary school (grades 1-4)	7 (26.9)	2 (7.7)
“Hauptschule” (grades 5-9)	1 (3.8)	-
“Realschule” (grades 5-10)	1 (3.8)	2 (7.7)
“Gymnasium” (grades 5-12 / 5-13)	8 (30.8)	13 (50.0)
Specialized schools*	7 (26.9)	4 (15.4)
Too young to attend school	2 (7.7)	-
Graduated from school	-	5 (19.2)

* including schools for physically disabled children, but not schools for children with intellectual disabilities.

„Realschule“ (grades 5-10) as an intermediate school to prepare mainly practically and theoretically oriented students for trade, technical and administrative professions, and “Gymnasium” (grades 5-12 or 5-13) as academic secondary school, preparing students to tertiary education or university. Alternatively, students can attend “Gesamtschule” (comprehensive school, grades 5-10). The range of public schooling modalities in Germany is completed by schools for students with special needs, e.g. physical or intellectual disability or disciplinary problems, comprising elementary and secondary school. According to data from the German Federal Statistical Office, the relative distribution of secondary school students in 2015 was: “Gymnasium”: 34.2%, “Realschule”: 22.7%, “Gesamtschule”: 15.8%, “Hauptschule”: 12.1%, others: 25.2% (Statistisches Bundesamt, 2016).

At follow-up assessment, 24 parents classed their child’s intelligence as at least average (compared to 23 at T1), one as below the average (learning disorder; same parent as at T1), but none as intellectually disabled. One parent could not make a decision compared to two parents at T1.

In all cases the primary caregiver was the child’s mother or father (no changes between T1 and T2). At T2, their mean age was 44.19 years (standard deviation: 4.67 years; range: 34-54 years; T1: mean: 40.12; SD: 4.65 years; range: 30-50 years). 23/26 parents lived together, one primary caregiver did not have a life partner (no changes between T1 and T2).

At T1, three primary caregivers had graduated from “Hauptschule”, seven from “Realschule”, and sixteen from “Gymnasium” of whom 6 had graduated from university. At T2 another three primary caregivers had graduated from university.

At T2, 7 primary caregivers were unemployed or housewife (compared to 9 at T1), the rest of the primary caregivers worked at least part time. 22/26 subjects with MS had at least one sibling (T1: 22/26). None of the primary caregivers rated the family’s financial situation as not sufficient (no changes between T1 and T2).

4.2. Psychological Adjustment

Regarding CBCL/ 4-18 results at T1, no statistically significant differences could be found between primary caregivers who only participated at T1 and primary caregivers who participated as well at T2.

For results of the CBCL/ 4-18 at both study times ($n = 20$, 10 females, 10 males) see Table 3.

One sample t -tests revealed statistically significantly higher t -scores on almost all CBCL/ 4-18 scales at T1 and T2 [exceptions: Thought Problems (T1) and Externalizing Problems (T 1 and T 2)] than in the general population. Effect sizes ranged from $d = 0.01$ (Externalizing Problems) to $d = 1.25$ (Social Problems) at T1 and from $d = 0.07$ (Externalizing Problems) to $d = 1.08$ (Withdrawn) at

Table 3

Mean T-scores, standard deviations, clinical and borderline cases of younger subjects at both study times (n = 20, 10 female, 10 male)

CBCL 4-18 scales	T1			T2		
	Mean T-score (SD; <i>d</i>)	Clinical cases (%)	Borderline cases (%)	Mean T-score (SD; <i>d</i>)	Clinical cases (%)	Borderline cases (%)
Total Problems	56.50 *** (7.40; 0.74)	1 ♀, 1 ♂ (10 %)	1 ♀, 1 ♂ (10 %)	57.70 ** (8.19; 0.84)	3 ♀, 1 ♂ (20 %)	2 ♀, 1 ♂ (15 %)
Internalizing Problems	58.00 *** (7.97; 0.88)	2 ♀, 2 ♂ (20 %)	4 ♂ (20 %)	58.80 *** (9.72; 0.89)	5 ♀, 3 ♂ (40 %)	1 ♀, 2 ♂ (15 %)
Externalizing Problems	49.95 (8.95; 0.01)	1 ♀, 1 ♂ (10 %)	1 ♀ (5 %)	49.35 (8.48; 0.07)	2 ♀ (10 %)	1 ♀ (5 %)
Withdrawn	58.35 *** (7.14; 0.96)	2 ♂ (10 %)	1 ♀ (5 %)	60.20 *** (8.87; 1.08)	1 ♀, 2 ♂ (15 %)	1 ♀, 1 ♂ (10 %)
Somatic Complaints	55.80 ** (8.09; 0.64)	3 ♂ (15 %)	-	55.55 *** (6.17; 0.67)	-	-
Anxious / Depressed	57.55 *** (8.91; 0.80)	2 ♀ (10 %)	3 ♂ (15 %)	59.60 *** (9.19; 1.00)	3 ♀, 1 ♂ (20 %)	1 ♂ (5 %)
Social Problems	60.75 *** (6.97; 1.25)	1 ♀, 1 ♂ (10 %)	1 ♀, 1 ♂ (10 %)	59.45 *** (8.62; 1.01)	2 ♀, 1 ♂ (15 %)	1 ♀ (5 %)
Thought Problems	52.50 (5.84; 0.31)	1 ♀ (5 %)	-	54.25 * (7.38; 0.48)	1 ♀ (5 %)	2 ♀ (10 %)
Attention Problems	54.95 * (7.86; 0.55)	1 ♂ (5 %)	1 ♀ (5 %)	55.75 ** (7.11; 0.66)	1 ♂ (5 %)	1 ♀ (5 %)
Delinquent Behavior	52.85 ** (4.26; 0.37)	-	-	52.20 ** (3.09; 0.30)	-	-
Aggressive Behavior	53.60 * (6.76; 0.42)	1 ♀ (5 %)	1 ♂ (5 %)	53.60 * (5.83; 0.44)	-	2 ♀ (10 %)

Note: One-sample t-test: * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$; SD: Standard deviation; *d*: Cohen's $d (M_1 - M_2 / \sigma_{pooled})$

T2 with mean effect sizes of .63 (T1) and .68 (T2).

11/20 (55.0 %), six females and five males, scored clinical on at least one of the CBCL/ 4-18 scales at T2, compared to 10/26 subjects (38.5%), seven males and three females, at T1.

By means of McNemar's test, no statistically significant changes between T1 and T2 could be found with regard to clinical scores of the CBCL/ 4-18 global scales Internalizing, Externalizing and Total Problems.

At T1 and T2, no statistically significant sex differences could be found. No significant correlations could be found between the subjects' age (in years) and the CBCL/ 4-18 scales at T1 and T2.

Results for subjects older than 18 years are given in Table 4. 2/6 subjects (33.3%), one male and one female, scored clinical on at least one of the YABCL/ 18-30 scales, the same two subjects had a total problem scale in the clinical range. These two subjects had already been rated clinical or borderline at T1.

To examine possible life stage effects on psychological adjustment we compared younger children (aged 4-9 years at T1; $n = 11$) with older subjects (aged 10-14 years at T1; $n = 9$) regarding CBCL/4-18 *t*-scores at T1 and T2. Additionally, for each subject a *t*-score difference between both assessment points was calculated. No statistically significant differences could be found between both

Table 4

Median T-scores, range, clinical cases and borderline cases of older subjects at both study times (n = 6, 4 female, 2 male)

T1: CBCL/ 4-18				T2: YABCL			
CBCL/ 4-18 scales	Median T-score (Range)	Clinical cases	Borderline clinical cases	YABCL scales	Median T-score (Range)	Clinical cases	Borderline clinical cases
Total Problems	42 (36-73)	1 ♂	1 ♀	Total Problems	42 (33-67)	1 ♀, 1 ♂	-
Internalizing Problems	47 (37-70)	1 ♂	1 ♀	Internalizing Problems	48 (35-78)	1 ♀, 1 ♂	-
Externalizing Problems	44 (31-63)	-	1 ♂	Externalizing Problems	42 (36-60)	-	1 ♀
Withdrawn	50° (50°-69)	-	1 ♂	Withdrawn	54 (50°-80#)	1 ♀	1 ♂
Somatic Complaints	50° (50°-58)	-	-	Somatic Complaints	50° (50°-62)	-	-
Anxious / Depressed	50° (50°-70)	-	1 ♂	Anxious / Depressed	51 (50°-70)	-	1 ♀, 1 ♂
Thought Problems	50° (50°-80#)	1 ♂	-	Thought Problems	50° (50°-77)	1 ♂	-
Attention Problems	50° (50°-80#)	1 ♂	-	Attention Problems	50° (50°-80#)	1 ♀	-
Delinquent Behavior	50° (50°-61)	-	-	Delinquent Behavior	50° (50°-60)	-	-
Aggressive Behavior	50° (50°-65)	-	-	Aggressive Behavior	50° (50°-58)	-	-
Social Problems	50° (50°-76)	1 ♀, 1 ♂	-	Intrusive	50° (50°-65)	-	-

° T-value equal to or smaller than 50, # T-value equal to or higher than 80

Table 5

FPI-R scales at T1 and T2: means, standard deviations, effect sizes, and clinical cases (T1: n = 26; T2: n = 25).

FPI-R scales	T1: Mean (SD; <i>d</i>)	T1: Clinical cases	T2: Mean (SD; <i>d</i>)	T2: Clinical cases
Strain	5.19 (2.70; 0.08)	4 (15.4 %)	5.04 (2.60; 0.02)	3 (12.0 %)
Life Satisfaction	5.04 (1.43; 0.02)	0 (0 %)	5.28 (1.54; 0.16)	0 (0 %)

Note: One-sample t-test: * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$; SD: Standard deviation; *d*: Cohen's d ($M_1 - M_2 / \sigma_{\text{pooled}}$)

groups.

4.3. Strain and life satisfaction

Regarding FPI-R subscales at T1, no statistically significant differences could be found between primary caregivers who only participated at T1 and primary caregivers who participated as well at T2.

Results of the FPI-R are shown in Table 5.

Significant differences could be found neither between the study group (at T1 and T2) and the general population (effect sizes for all subscales were below 0.2) nor between FPI-R scores at T1 and T2. No significant differences between primary caregivers of boys and girls could be found for any of the FPI-R subscales at T1 and T2. The child's age (in years) did not show any significant correlation with the FPI-R subscales at T1 and T2.

Significant correlations could be found between strain and life satisfaction (T1: $r = -0.749$, $p \leq 0.001$; T2: $r = -0.514$, $p = 0.009$).

Strain also correlated significantly with all three global scales of the CBCL/ 4-18 at T1 (Internalizing Problems: $r = 0.457$; $p = 0.019$; Externalizing Problems: $r = 0.473$, $p = 0.015$; Total Problems: $r = 0.503$, $p = 0.009$). At T2 a significantly positive correlation could be found between strain and the global scales Internalizing problems ($r = 0.520$; $p = 0.019$) and Total Problems ($r = 0.508$, $p = 0.022$).

4.4. Comparison of psychological adjustment, parental strain, and life satisfaction between T1 and T2

Regarding CBCL/ 4-18 and the FPI-R subscales, no significant changes with time could be found. Additionally, no significant interactions of CBCL scales with time or FPI baseline values could be found by means of MANOVA. All effect sizes were about zero.

5. Discussion

To the authors' best knowledge, this is the first longitudinal study on psychological adjustment in subjects with MS and their primary caregivers' strain and life satisfaction. For this purpose, well-validated assessment instruments were applied.

26 out of 31 (83.9 %) of the addressed primary caregivers who had already participated in a first study (Briegel, Schimek et al., 2010) returned filled-out questionnaires, which is a very satisfactory result. Compared with the study of Verzijl et al. (2003) lower rates of bilateral facial paralysis and malformations of feet and hands have been reported, which might be due to different ways of information acquisition (by parents in this study versus by means of physical examination in the study of Verzijl and colleagues). Another possible explanation could be that our sample constitutes a selection of milder cases of MS. The fact that neither parent rating nor schooling modality indicated intellectual disability in our study sample and that a disproportionately high number of subjects with MS attended the prestigious "Gymnasium" at T2 might support the latter explanation.

Regarding psychological adjustment, both at T1 and T2, the subjects with MS included in this study scored significantly higher on almost all CBCL/ 4-18 scales than age and sex matched subjects of the general population. High effects were found at T1 and T2 for the following CBCL/ 4-18 scales: Internalizing Problems, Withdrawn, Anxious/Depressed, and Social Problems. Rates of clinical internalizing (T1: 19.2%, T2: 38.5%) and total problems (T1: 11.5%, T2: 23.1%) increased with time, but these increases did not reach statistical significance. Similarly, 55 % of the subjects were rated clinical on at least one of the CBCL scales at T2 compared to 38.5 % at T1. As 45% (at T2) to 61.5% (at T1) of our sample of young subjects with MS were not rated clinical on at least one CBCL scale, our data reveal that psychological adjustment is not generally impaired in young subjects with MS, but that a considerable percentage might develop clinical adjustment problems, especially internalizing ones. These findings correspond to high rates of major depression and suicidal thoughts in adults with MS as reported by Briegel (2007). However, results for adult subjects are inconclusive with regard to depression and satisfaction with life (Bogart & Matsumoto, 2010; Briegel, 2007).

Although rates of clinical adjustment problems suggest an increase with age, no statistically significant intra-individual differences could be found between CBCL scores at both study points. We could also find no life stage effects. Moreover, primary caregivers did not report on significant increases in psychiatric disorders, psychopharmacological or psychotherapeutic interventions over time. Last but not least, no significant correlations of CBCL scales with the subjects' age could be found. This latter finding is in contrast to results of the first study (Briegel, Schimek et al., 2010) which suggested an increase of social problems with age.

Thus, our data do not show a uniform or systematic tendency that adjustment problems in young subjects with MS may be more

pronounced with growing age, a finding which corresponds to results of [Strobel and Renner \(2016\)](#) emphasizing the importance of longitudinal data for reliable conclusions. One possible reason for the discrepant findings in our study might be that the sample that could be used for statistical calculations ($n = 20$) was significantly smaller than the sample used for categorization ($n = 26$) resulting in reduced statistical power.

Regarding parental strain we found clinical levels about three times (T1: 15.4 %, T2: 12.0 %) as frequently as in the age and sex matched general population (4%) while a one-sample *t*-test revealed no significant differences compared to the general population (effect sizes below 0.1). No significant changes between both study points could be found, and parental strain was independent from the child's sex. However, strain was significantly positively related to the CBCL/ 4-18 global scales Total Problems and Internalizing Problems at T1 and T2, findings which are in accordance with the results of other authors. [King, King, Rosenbaum, and Goffin, \(1999\)](#) found child adjustment problems to be the single most important predictor of caregivers' psychological well-being. Moreover, [Baker et al. \(2003\)](#) showed that parenting stress is related to the extent of behaviour problems rather than to the child's developmental delay.

Strain also showed a significantly negative correlation with the primary caregiver's life satisfaction. However, levels of life satisfaction were similar to age and sex matched people, both at T1 and T2, results that are partially in line with previous studies ([Briegel et al., 2007](#); [Briegel, Hofmann et al., 2010](#)). As nearly all parents of our study group lived together at T1 and T2, and the psychosocial situation remained quite stable for most subjects with MS, we suppose that partnership support could have contributed to normal levels of satisfaction with life. This hypothesis is supported by studies which showed that partnership support is the best predictor of coping for mothers of children with disabilities ([Lambrenos, Weindling, Calam, & Cox, 1996](#)). Mastery has been repeatedly shown to be associated with both physical and psychological health in different populations ([Caplan, 1981](#); [Ransom, Fisher, & Terry, 1992](#)). Thus, if the caregiver is able to master problems, e.g. by social support and / or intrapsychic coping strategies like cognitive reframing, life satisfaction can be quite normal ([Barakat & Linney, 1992](#)). Longitudinal data of this study revealed neither significant changes on the FPI-R subscale life satisfaction nor significant interactions with time, whereas the original cross-sectional study by [Briegel, Hofmann et al. \(2010\)](#) found a significantly positive correlation between the age of subjects with MS and their primary caregivers' life satisfaction.

6. Limitations

Despite clear strengths, including the longitudinal design with a strong follow-up rate, carefully chosen clinically relevant measures and a sample size which is among the largest of this rare population, this study has some limitations. A methodological limitation is the lack of a matched control group. Generalizability is further limited due to the questionable representativeness of our study sample. One reason for questionable representativeness is the fact that we used a convenience sample of participants. Therefore sample selection bias cannot be excluded. A second reason is the inclusion rate for this longitudinal study of only 44.8 % of all subjects with MS aged 4-17 years who were originally known to the German MS foundation. As questionnaires were sent anonymously, we do not have any information about subjects whose caregivers did not follow our request to participate in this study. However, as there is no central register for MS in Germany and in most other countries, the true prevalence of MS remains unclear and questionable representativeness applies to almost all studies on MS.

Another limitation is the small number of subjects included in this follow-up study ($n = 26$) which certainly resulted in limited statistical power for all analyses. However, as MS is a very rare congenital condition, up to date the largest studies on subjects with MS comprised only 37 subjects ([Bogart & Matsumoto, 2010](#); [Verzija et al., 2003](#)) with a wide age range. In contrast, this follow-up study included only subjects aged 8 to 21 years.

A last limitation is the lack of objective information on the subjects with MS (e.g. on their intelligence) and the fact that we used only parent-report measures. Self-report instruments might have revealed different results ([Briegel, 2012](#)) and should be included in further longitudinal studies.

7. Conclusion

Although many subjects with MS seem to master social problems by means of intrapsychic coping strategies and support by their family and friends ([Meyerson, 2001](#)), clinical adjustment problems, especially internalizing problems, seem to be very frequent among young subjects with MS, at least according to their primary caregivers perception. Moreover they seem to increase with time. The fact that we could not find statistically significant changes with time is probably the consequence of our small study sample.

In spite of elevated rates of clinical levels of strain among caregivers of children and adolescents with MS, neither life satisfaction nor parental strain was significantly different when compared to the general population. Moreover, primary caregivers' strain and life satisfaction did not show significant changes with time. However, careful monitoring as well as early and adequate interventions, if indicated, should be offered to families with a child with MS, not only for somatic complaints but also for problems with psychological adjustment. Apart from one exploratory study ([Michael et al., 2015](#)), which showed that training in compensatory strategies might be helpful in teenagers with MS, there have been no effectiveness studies on the prevention and treatment of psychiatric disorders in subjects with MS so far. Thus, interventions, e.g. cognitive behaviour therapy for internalizing disorders in older children and adolescents, should be chosen in accordance with the guidelines of the psychological and psychiatric scientific societies. Additionally, contact to and support by the Möbius foundation can be helpful for many families with a child with MS ([Briegel, 2006](#)).

Acknowledgements

The authors are very grateful to Moebius Syndrom Deutschland e.V., the German Moebius association, and to all parents who participated in this study.

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