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No impact of adult attachment and temperament on clinical variability in patients with clinically isolated syndrome and early multiple sclerosis

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ABSTRACT

Objective: Attachment style and temperament could influence a stress–relapse relationship in multiple sclerosis. We therefore aimed to probe for an association of these personality-related variables with disease activity in patients with clinically isolated syndrome and early multiple sclerosis (MS). *Methods:* Study participants completed following psychometric instruments: Adult Attachment Scale (AAS), Temperament and Character Inventory (TCI-125), Hospital Anxiety and Depression Scale (HADS). Clinical data encompassed the expanded disability status scale (EDSS), annualized relapse rate, disease duration and therapy. Relapses and MRI data were recorded at regular outpatient visits.

Results: Study participants (n = 84), 38 with a clinically isolated syndrome suggestive of MS (CIS) and 46 with relapsing remitting MS (RRMS), were assessed with a low EDSS (median 2). No significant differences concerning personality-related variables were revealed by group comparisons between CIS and RRMS and within the RRMS subgroup based on clinical measures (EDSS/year; within RRMS subgroup: annualized relapse rate). However, a higher lesion load per years of disease duration within the RRMS subgroup was associated with higher values in the temperament trait harm avoidance (p < 0.05).

Conclusions: Although harm avoidance may be related to subclinical disease activity in early RRMS adult attachment and temperament do not seem to contribute to differences between CIS and RRMS or clinical variability in early multiple sclerosis.

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1. Introduction

Multiple sclerosis (MS) is the most frequent chronic demyelinating disease of the central nervous system. The incidence rates of MS have the highest peak in the third and fourth decade. Most (85%) patients have a relapsing remitting form of the disease [1]. A first attack suggestive of MS is currently diagnosed as clinically isolated syndrome (CIS) [2]. Yet, not all patients with a CIS continue to develop symptoms and are then diagnosed as clinically definite MS [2,3].

Psychological stress appears to play some role in the course of relapsing remitting multiple sclerosis (RRMS). In a meta-analysis, Mohr et al. demonstrated a small but consistent relationship between stressful life events and relapse rate [4]. All included

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studies showed an increased risk of exacerbation for moderate stressors. In a two-year prospective study by Brown et al., relapses were predicted by the number of acute moderate stressors and by coping behaviours that focused on seeking social support [5]. They were not predicted by depression, anxiety, subjective fatigue, cognitive test performance, health locus of control, optimism, social support, lifestyle factors (e.g. exercise, substance use) or other coping behaviours than seeking social support. All this argues for an association between stress and MS exacerbation but the exact mechanism(s) involved is still unclear. In this context the suggested stress-relapse relationship could be influenced by a third variable, such as an underlying dispositional or personality factor [6]. Adult attachment style and temperament deserve particular interest in this respect. They imply specific individual psychobiological response patterns to stressful life events and are thus assumed to influence health and disease [7-11].

Attachment theory postulates an innate, evolutionarily grounded motivational system designed to promote and maintain some key relationships from infancy to old age [12]. Attachment style develops in infancy, based on a child's relationship with

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his or her primary caregiver, and usually affects an individual's close relationships throughout life. It can be described by two underlying dimensions which differentiate between secure and insecure attachment: attachment related anxiety and attachment related avoidance. If, for example, confronted with the diagnosis of a potentially disabling disease, securely attached individuals will rather assume social support to be available for them. They will thus experience less stress with less frequent activation of their stress systems than insecurely attached individuals [12]. Accordingly, secure attachment is regarded as a health protective factor [8]. Conversely, insecure attachment has been linked to worse clinical courses, e.g. in migraine and ulcerative colitis, pointing to a potentially broader clinical relevance of this theory [13,14].

While attachment style refers to interpersonal behaviour temperament traits imply more general behavioural tendencies. Cloninger's psychobiological model of personality comprises the four temperament traits harm avoidance, novelty seeking, reward dependence and persistence [9]. These traits are assumed to represent a biological core for personality development and to have substantial impact on an individual's psychobiological stress response [15]. In particular harm avoidance has been reported to influence health and disease. More specifically, high harm avoidance was found to be negatively correlated with resilience [8], to have a negative impact on the course of migraine [16], to be positively correlated with the severity of bradykinesia and depression in Parkinson's disease [17], but also, in contrast, to be protective towards development of atherosclerosis [18].

Attachment style and its possible implications have not yet been studied in patients with MS. However, one study has dealt with temperament traits in this patient group [19]. This study suggested increased harm avoidance, decreased reward dependence and reduced persistence in MS patients compared to healthy controls. We therefore decided to probe whether dimensions of adult attachment and temperament traits, in particular insecure attachment and harm avoidance, differed between and within disease stages. We intended to focus on early stages of the disease to keep the influence of secondary effects of the clinical course on the investigated personality variables as small as possible.

Thus, our first study aim was to compare the distribution of dimensions of adult attachment and temperament traits between patients with a clinically isolated syndrome suggestive of MS (CIS) and patients with definite relapsing remitting MS (RRMS). In this comparison of clinical subgroups we hypothesized to find higher values of attachment insecurity and harm avoidance in patients with RRMS as compared to patients with a CIS. Our next study goal was to explore if the investigated personality variables were associated with measures of clinical and subclinical disease activity. In this respect MRI-based data were intended to complement clinical data as a biological surrogate marker of disease activity.

2. Methods

Study participants were consecutively and prospectively enrolled from our MS outpatient department following ethical committee's approval. Inclusion criteria were a diagnosis of a CIS [2] or of RRMS [20], and the patient's willingness, capacity and written consent to undergo detailed clinical and psychological testing and 3T MRI. Over a period of 22 months 84 persons fulfilled these criteria and could be included in the study.

2.1. Sociodemographic data and disease activity

Demographic and clinical data recorded included age, gender, age at disease onset, disease duration, and treatment. In both

patients with CIS and RRMS disease duration was defined as the interval between the first clinical attack and the assessments for this study. Disability was measured with the expanded disability status scale (EDSS) [21]. For the RRMS subgroup disease activity was assessed in three additional ways. First, from the documented previous relapses at regular outpatient visits, an annualized relapse rate was calculated. Relapses were defined as the appearance or reappearance of at least one neurological symptom or as the worsening of an old symptom attributable to MS that lasted for at least 24h and was preceded by a relatively stable or improving neurological state of at least 30 days. Second, as another clinical measure of disease activity we also calculated the progression index (PI) defined as the EDSS in relation to disease duration in years. Finally, analogue to the PI, we calculated a ratio between T2 lesion volume and years of disease duration as an MRI-based measure of disease activity. MRI data were obtained at 3 T MRI (Siemens Tim Trio, Siemens Healthcare, Erlangen, Germany) using a phasedarray head coil with 12 receive elements and a consistent imaging protocol [22]. All image analyses were performed by trained and experienced technicians and interpreters, blinded to clinical information. As previously reported for assessing T2 lesion load [22,23], masks defining the lesions were created using "DispImage", an image processing software provided by David Plummer, University College, London, UK, which has been described in detail elsewhere [24]. Then the total lesion load was calculated by multiplying the area of all masks by the slice thickness.

2.2. Psychometric variables

Study participants completed all psychological instruments at study entry. The revised German version of the Adult Attachment Scale (AAS) [25] was used to explore the following three dimensions inherent in adult attachment style: attachment closeness (describing the extent to which an individual feels comfortable with closeness), attachment confidence (referring to the extent to which subjects can trust others and depend on them when needed) and attachment anxiety (reflecting anxiety in relationships, such as the extent of fear of being abandoned and not being loved). According to Collins and Read a person with a secure attachment style can be assumed to be comfortable with closeness, able to depend on others and trust in them, and not to be worried about being abandoned or unloved [26]. We decided to choose the AAS because this instrument is recommended to be used in clinical research, in particular for exploring bio-psychosocial interrelations [25].

The German version of the short form of the Temperament and Character Inventory (TCI-125) was used to measure Cloninger's dimensions of personality [9,28]. The four basic biologically influenced temperament traits of this model refer to behavioural tendencies. Harm avoidance (HA) is defined as a tendency to avoid negative stimuli by behavioural inhibition. Reward dependence (RD) describes a tendency to maintain behaviour that has been experienced as being socially rewarded. Novelty seeking (NS) reflects behavioural activation and a tendency to strongly react to novel stimuli. Persistence (P) describes a tendency to act persistently despite frustrating experiences. The TCI-125 also measures the three dimensions of character of Cloninger's psychobiological model of personality: self-directedness (SD), cooperativeness (C) and self-transcendence (ST). In contrast to temperament traits that imply automatic emotional reactions and according behavioural tendencies, these dimensions of character reflect self-concepts about goals and values. They can modify the significance and meaning of what is experienced and thus also change behavioural habits. Self-directedness expresses the degree to which the self is experienced as autonomous and capable of self-regulation, cooperativeness reflects the degree to which the self is oriented towards

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