

ABSTRACT

Background: Environmental risk factors such as early life stress (ELS) are associated with an increased risk to develop affective and non-affective psychosis^{1,2}, an earlier onset of illness and worse social functioning³. Childhood abuse and neglect are known to have a negative influence on cognition in patients with schizophrenia⁴. However, the effects of childhood trauma on long-term outcome and underlying neurobiological mechanisms are unknown.

Methods: We explored phenotypic data (early life stress, cognition, psychopathology and functioning) from the longitudinal PsyCourse study. The selected sample comprised 87 patients with schizophrenia (DSM-IV) with ELS and 82 patients without ELS. ELS was assessed using the childhood trauma screener. We investigated whether ELS-patients show impairment in neuropsychological tests (TMT-A & B, DST, VLMT), psychopathology (PANSS), severity of the illness (CGI) and global functioning (GAF).

Results: ELS had a significant impact on a subset of the analyzed variables. Adjusted for age, treatment and level of education, the length of time required for the trail-making-test (TMT-A & B) was significantly longer in ELS compared to no-ELS patients ($p = 0.001$ and $p = 0.005$). For the group of inpatients or day patients, ELS patients had higher PANSS total scores ($p = 0.030$), lower CGI scores ($p = 0.004$) and more severe functional impairment (GAF) ($p = 0.001$) (Figure 3). A worse social functioning associated with ELS couldn't be observed in the group of outpatients or patients without current treatment.

Discussion: ELS is associated with cognitive impairment, increased psychopathology and worse level of functioning in patients with schizophrenia. In a second step, we will repeat the analyses in a larger sample including healthy controls. Furthermore, we will perform a microRNAome approach to investigate the underlying neurobiological mechanisms.

BACKGROUND

Environmental risk factors such as early life stress (ELS) are associated with an increased risk to develop affective and non-affective psychosis^{1,2}, an earlier onset of illness and worse social functioning³. There are five different types of trauma such as physical abuse and neglect, emotional abuse and neglect and sexual abuse. Robust data on the epidemiology of trauma types and their impact on the onset and course of affective and non-affective psychosis are scarce. Most research into this field concentrated on physical and sexual abuse. But there are indications that emotional abuse and neglect have the highest prevalence among trauma subtypes⁵⁻¹⁰. Schizophrenia patients experienced more frequent emotional neglect, but also physical abuse and physical neglect^{11,12}. Concerning course and outcome childhood abuse and neglect are known to have a negative influence on cognition in patients with schizophrenia⁴. It leads to reduced scores on working memory, executive function, verbal memory and attention^{11,12}. However, the effects of childhood trauma on long-term outcome and underlying neurobiological mechanisms are unknown.

METHODS

Participants

Longitudinal data was used from the PsyCourse study in Germany and Austria (www.PsyCourse.de)¹³. Participants were phenotyped using a comprehensive battery including data on socio-demographics, history of illness, early life stress (Childhood Trauma Screener¹⁴), psychopathology (PANSS) and cognition. The Cognitive tests included the Trail-Making-Test A & B (TMT-A & B), Verbal Learning and Memory Test (VLMT) and the Digit-Symbol-Test (DST). Social functioning was measured with Global Assessment of Functioning (GAF) and Clinical Global Impression Scale (CGI).

Independent variable

Early life stress: ELS was assessed using the childhood trauma screener, a five-point scale containing the five types of childhood trauma. The selected sample comprised 87 schizophrenia patients with ELS and 82 patients without ELS according to validated threshold values¹⁵.

Dependent variables

Cognition: time required for TMT-A & B (logarithmic transformed), score from DST and score of total correct answers from the VLMT (logarithmic transformed).

→ ANCOVA: between-subject factors group (ELS, no-ELS) adjusting for level of education and age
Psychopathology and social functioning: PANSS, CGI and GAF

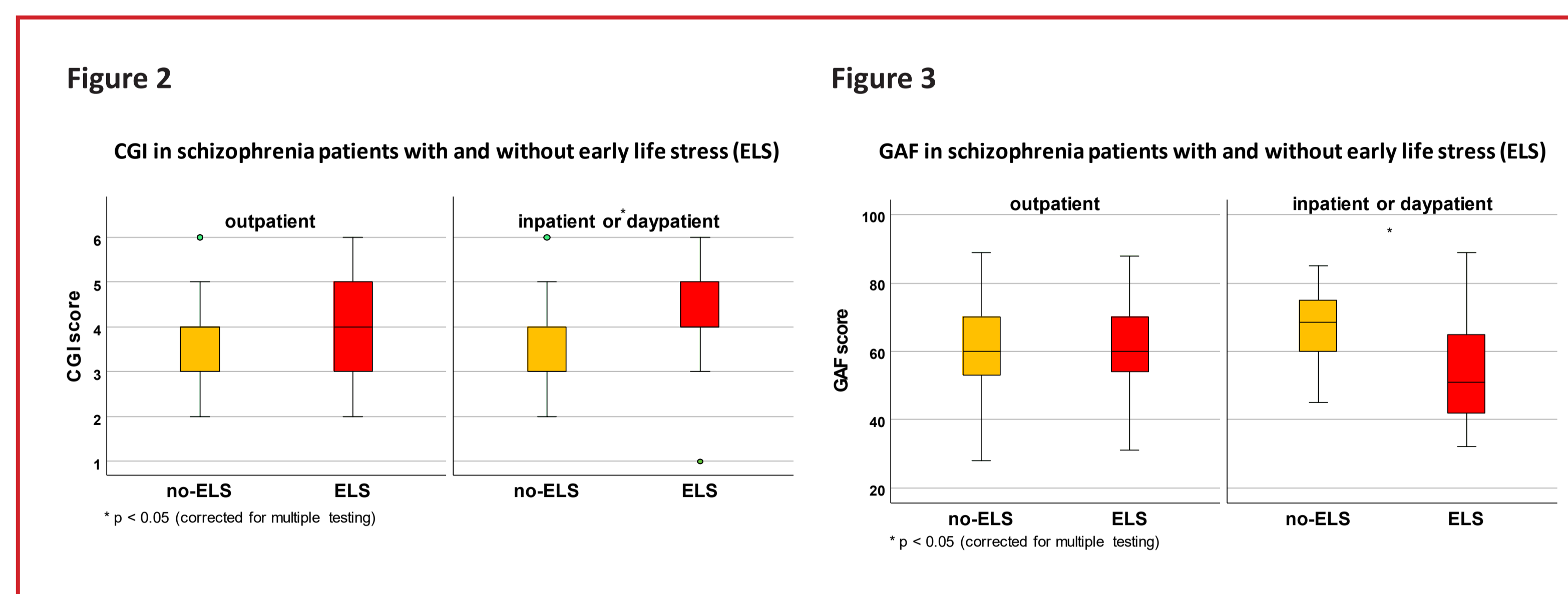
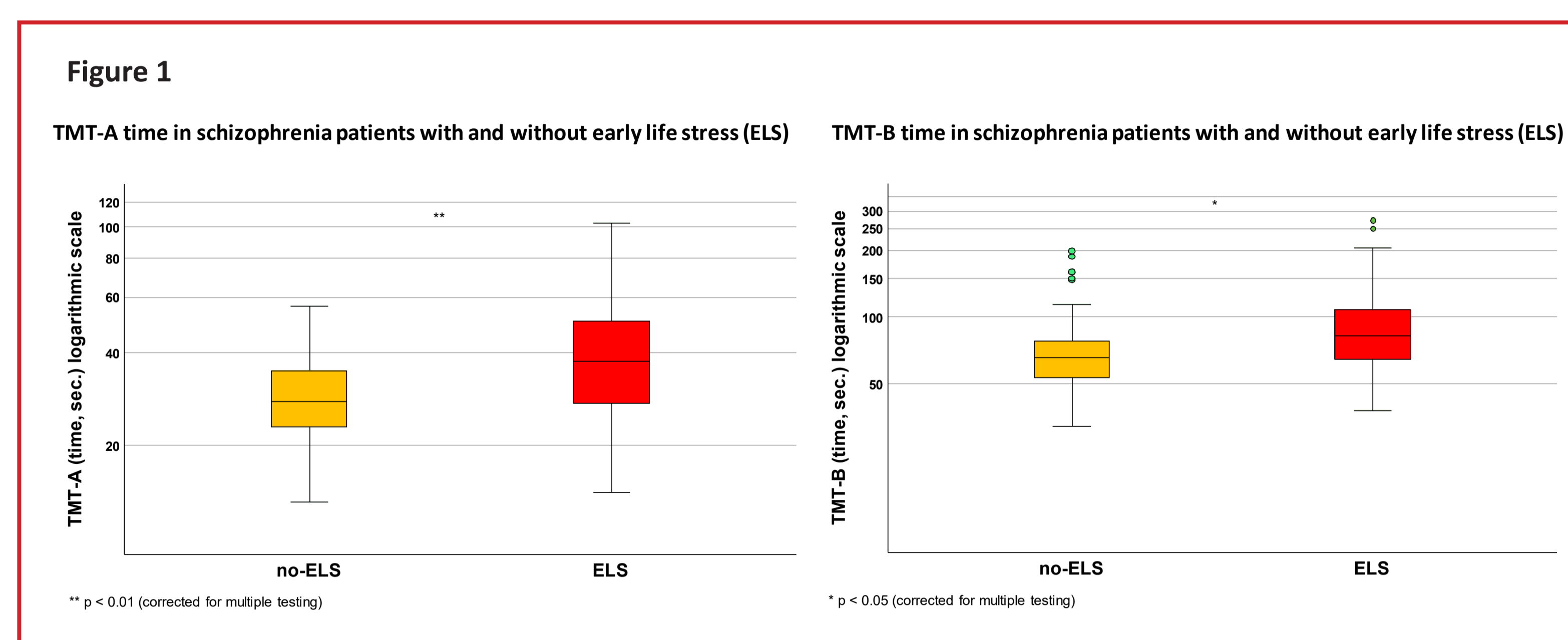
→ Non-parametric Mann-Whitney U tests to compare ELS and no-ELS patients separately for the two treatment groups (inpatients or day patients vs. outpatients or no treatment)

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RESULTS

ELS had a significant impact on a subset of neuropsychological domains. Adjusted for age, treatment and level of education, the length of time required for the TMT-A and TMT-B was significantly longer in ELS compared to no-ELS patients ($p = 0.001$ and $p = 0.005$) (Figure 1). There was no significant difference in the DST and VLMT between ELS and no-ELS patients, although numerically ELS patients showed a worse mean test performance in the DST and to a lesser extent also in the VLMT. For the group of inpatients or day patients, ELS patients had higher PANSS total scores ($p = 0.030$), lower CGI scores ($p = 0.004$) (Figure 2) and more severe functional impairment (GAF) ($p = 0.001$) (Figure 3). A worse social functioning associated with ELS couldn't be observed in the group of outpatients or patients without current treatment.



DISCUSSION

ELS is associated with cognitive impairment, increased psychopathology and worse level of functioning in patients with schizophrenia. The increased value of the TMT-A indicates impairment of the processing speed, the increased value of the TMT-B suggests limitations in the area of higher cognitive performance, such as mental flexibility. VLMT measures declarative verbal memory, DST learning and processing speed. Both differentiate in the lower power range. To conclude, ELS seems to have a negative effect on executive functions such as processing speed and higher cognitive performance in patients with schizophrenia.

In a second step, we will repeat the analyses in a larger sample including healthy controls. Furthermore, we will add data on depressive symptoms and medication to the analyses. As the the PsyCourse sample comprises genetic data we will perform a microRNAome approach to investigate the underlying neurobiological mechanisms.

Table 1 Demographics of schizophrenia patients with and without ELS

	no-ELS			ELS			F	df	p
	N	mean	Sd	n	mean	sd			
Age (years)	82	41.2	11.7	87	44.4	12.3	3.1	1,167	0.081
Disease Duration (years)	82	12.7	8.5	84	15.6	11.7	3.3	1,164	0.070
	no. per category	no. per category		Chi²	df	p			
Gender male / female	56 / 26			56 / 31	0.3	1	0.59		
Treatment outpatient or no treatment / inpatient or day patient	60 / 22			54 / 33	2.4	1	0.12		
Marital Status married / living separate or divorced / single	15 / 7 / 59			11 / 22 / 52	8.7	2	0.013		
Level of education main school or no graduate / secondary school / high school	15 / 21 / 42			28 / 29 / 29	7.2	2	0.027		
Living Status not living alone / living alone	41 / 41			42 / 45	0.1	1	0.82		
Family history of psychiatric diseases no / yes	24 / 53			22 / 58	0.3	1	0.61		

X² for categorical variables and ANOVA for comparison of continuous variables