

Differential resting-state connectivity in depressed adolescents before and after psychotherapeutic treatment and compared to healthy controls

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Introduction

Adolescence is a vulnerable period for the development of psychiatric disorders such as depression which often shows a chronic course with relapses in adulthood (Patton et al. 2014). Investigating the neural correlates of psychiatric disorders early in life offers the opportunity to bypass effects of previous medication and/or by changes in neural processing due to a chronic course of a disorder (Cullen, 2012). Psychotherapeutic treatment effects are only sparsely investigated in adults (Fu et al. 2008) and even less empirical investigations exist in adolescents (Straub et al. 2015). In this study, we compared neural connectivity, measured by means of resting state magnetic resonance imaging (rsfMRI), of adolescent patients with depression (PAT) and matched healthy controls (HC) and analysed pre-to-post connectivity changes of PAT after participation in a brief cognitive behavioural group psychotherapy (CBT).

Methods

Study Design

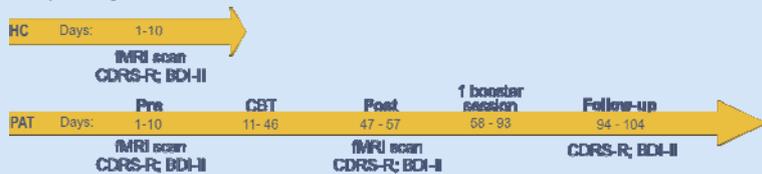


Figure 1 Study design CBT = cognitive behavioral therapy; PAT = depressed patients that received CBT; CDRS-R = Children's Depression Rating Scale Revised; BDI-II = Beck Depression Inventory- Revision; fMRI = functional magnetic resonance imaging

Inclusion criteria CDRS-R sumscore ≥ 36 ; Diagnosis of a depressive episode according to ICD-10; comorbidities were allowed (except for schizophrenia, bipolar disorder and substance abuse); no contradictions to fMRI scans; age between 13 and 18 years; IQ within normal range; medication naive

Subjects

	PAT (N=19) M \pm SD	HC (N=19) M \pm SD	Significance
Age (years)	16.76 \pm 1.39	16.35 \pm 1.47	n.s. ^a
Gender	15 females (79%)	15 females (79%)	n.s. ^b
Handedness ¹	18 right-handed (94.7%)	17 right-handed (89.5%)	n.s. ^b
IQ	98.39 \pm 7.53	102.61 \pm 12.33	n.s. ^a
Depression subtypes ²	Depressive disorder, mild (N=3); moderate (N=12); severe (N=4)	none	
Secondary diagnosis ²	Social phobia (N=4); Specific phobia (N=1); Attention deficit without hyperactivity (N=1); Socialized conduct disorder (N=1)	none	
Smoker	7 (36.8%)	1 (5.3%)	p=.02 ^b

Table 1 ¹ Edinburgh Handedness Inventory; ² Diagnosis according to ICD-10; ^a Wilcoxon's test; ^b chi-square test; n.s. = not significant

Diagnostic instruments: Children's Depression Rating Scale-Revised (CDRS-R); Beck-Depression Inventory Revision (BDI-II)

Psychotherapeutic treatment: CBT comprising five sessions á 75-90 minutes and one booster session (Spröber et al. 2012).

fMRI paradigm: resting state; Functional connectivity was calculated using SPM8 and the DPRSF toolbox on the whole brain level for spherical seed regions of interest (Amygdala, sgACC) based on previous studies, investigating differential connectivity with these regions between depressed and healthy adolescents

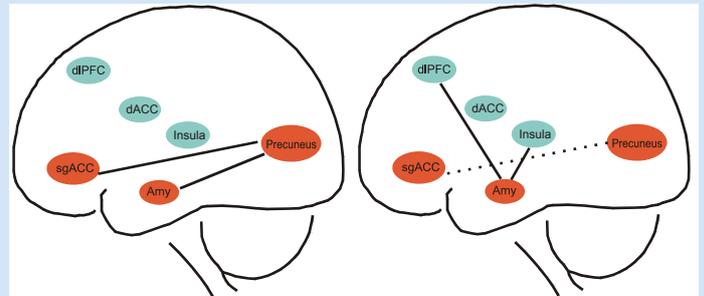
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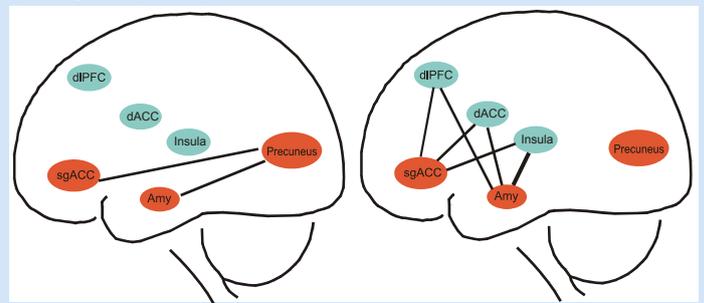
Results

Clinical symptoms PAT and HC differed with respect to the mean pre-test CDRS-R ($W_s = 190$, $z = -5.28$, $p < .001$) and BDI-II ($W_s = 194$, $z = -5.16$, $p < .001$). Within group analyses revealed significant pre-to-post reductions in the CDRS-R $F(1,18) = 13.93$, $p = .002$ and BDI-II $F(1, 18) = 10.94$, $p = .004$ for PAT (Straub et al 2015).

Comparing PAT and HC

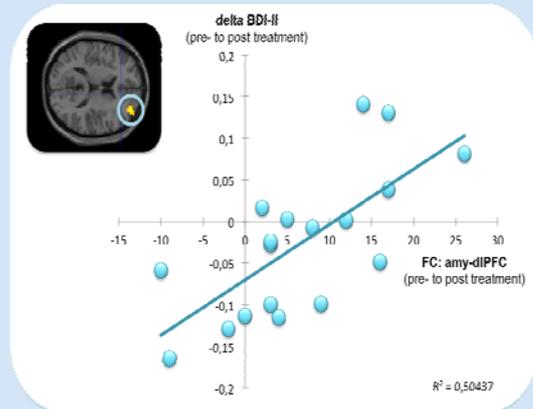


Comparing PAT pre to post



Notes dashed line indicates hypoconnectivity; straight line indicates hyperconnectivity; regions of the affective network (sgACC, Amygdala) and default mode network (precuneus) are depicted in red; regions of the cognitive control network (dACC, insula) and the salience network (dlPFC) are depicted in green; dlPFC=dorso lateral prefrontal cortex; dACC=dorsal anterior cingulate cortex; sgACC=subgenual anterior cingulate cortex; Amy=Amygdala

Correlation between symptom improvement and connectivity changes pre- to post CBT



Conclusions

Comparing functional connectivity of PAT after compared to before CBT revealed greater connectivity between emotionally relevant regions of the affective network (amygdala, sgACC) with regions of both, the salience network (dlPFC) and cognitive control network (dACC, insula). This indicates an increased top-down regulation in PAT post- compared to pre-CBT which can be interpreted as greater inhibitory control over neural circuits that process emotions after successful treatment. This might be due to specific CBT-techniques used, specifically addressing particularly dysfunctional cognitions and improvement of emotion control.

