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Sensory gating in adult with attention-deficit/hyperactivity disorder: Event-evoked potential and perceptual experience reports comparisons with schizophrenia

Jean-Arthur Micoulaud-Franchi ^{a,b,c,*}, Florence Vaillant ^d, Régis Lopez ^{e,f}, Pauline Peri ^d, Alexandra Baillif ^d, Laura Brandejsky ^d, Marie Laure Steffen ^{a,d,g}, Laurent Boyer ^{d,h}, Raphaëlle Richieri ^{d,h}, Michel Cermolacce ^{a,d,g}, Stéphanie Bioulac ^{c,i}, Mitsuko Aramaki ^j, Pierre Philip ^{b,c}, Christophe Lancon ^{d,h}, Jean Vion-Dury ^{a,d,g}

Background: In daily life, adults with attention-deficit/hyperactivity disorder (ADHD) report abnormal perceptual experiences that can be related to sensory gating deficit. This study investigated and compared P50 suppression (a neurophysiological measure of sensory gating) and perceptual abnormalities related to sensory gating deficit in ADHD and schizophrenias patients.

Methods: Three groups were compared: 24 adults with ADHD, 24 patients with schizophrenia and 24 healthy subjects. The Sensory Gating Inventory (SGI), a validated self-report questionnaire, was used to measure perceptual abnormalities related to sensory gating deficit. P50 suppression was measured by P50 amplitude changes in a dual-click conditioning-testing auditory event-related potential procedure.

Results: Adults with ADHD had significantly higher scores on the SGI and significantly lower P50 suppres-sion than healthy subjects. These deficits were similar to those found in patients with schizophrenia. A correlation was found between both the SGI and P50 suppression data in adults with ADHD and patients with schizophrenia.

Discussion: The findings confirm previous results found in patients with schizophrenia. Moreover, adults with ADHD, similar to patients with schizophrenia, had abnormal P50 suppression and reported being flooded with sensory stimuli. Abnormal neurophysiologic responses to repetitive stimuli gave rise to clinically abnormal perceptions.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent psychiatric disorders; the estimated prevalence ranges from 3% to 5% in adults (Caci, Morin, & Tran, 2014; Fayyad et al., 2007; Hudziak, Althoff, Derks, Faraone, & Boomsma, 2005). Inattention, hyperactivity and impulsivity are the core symptoms

^a Unité de Neurophysiologie et Psychophysiologie, Pôle de Psychiatrie Universitaire, CHU Sainte-Marguerite, 270 Bd Sainte-Marguerite, 13009 Marseille, France

b Services d'explorations fonctionnelles du système nerveux, Clinique du sommeil, CHU de Bordeaux, Place Amélie Raba-Leon, 33076 Bordeaux, France

^c USR CNRS 3413 SANPSY, CHU Pellegrin, Université de Bordeaux, Talence, France

d Pôle de Psychiatrie "Solaris", Centre Hospitalier Universitaire de Sainte-Marguerite, 270 Bd de Sainte-Marguerite, 13009 Marseille, France

^e Service de Neurologie, Unité des Troubles du Sommeil, Hôpital Gui-de-Chauliac Montpellier, Montpellier, France

f Inserm U1061, Montpellier F-34000 France

E Laboratoire de Neurosciences Cognitives (LNC), UMR CNRS 7291, 31 Aix-Marseille Université, Site St Charles, 3 place Victor Hugo, 13331 Marseille Cedex 3, France

h Laboratoire de santé publique évaluation des systèmes de soins et santé perçue, Université de la Méditerranée—EA 3279—Faculté de Médecine, 27 bd Jean Moulin, 13385 Marseille Cedex 05, France

ⁱ Pôle Universitaire de Psychiatrie de l'Enfant et de l'Adolescent, Bordeaux, France

Laboratoire de Mécanique et d'Acoustique, LMA, CNRS, UPR 7051, Aix-Marseille Univ, Centrale Marseille, F-13402 Marseille Cedex 20, France

^{*} Corresponding author at: Pôle de Psychiatrie "Solaris", Centre Hospitalier Universitaire de Sainte-Marguerite, 270 Bd de Sainte-Marguerite, 13009 Marseille, France. Tel.: +0033 0 622 364 019.

E-mail address: jarthur.micoulaud@gmail.com (J.-A. Micoulaud-Franchi).

of ADHD (American Psychiatric Association, 2000). Inattention may be related to an inability to control sensitivity to sensory stimuli (Venables, 1964). Patients with ADHD report being flooded with sensory stimuli; therefore, attention and information processing may be deficient in ADHD (Biederman, 2005; Faraone et al., 2000). The attention of patients with ADHD may be involuntarily drowned by many irrelevant environmental stimuli leading to impaired attention on relevant stimuli (Olincy et al., 2000). This hypothesis can be related to a sensory gating deficit. Sensory gating is the ability to filter intrusive sensory information, which is a specific and elementary form of pre-attentive information processing (Braff & Geyer, 1990). Sensory gating may protect higher cognitive function from flooding by irrelevant sensory information (Venables, 1964). Sensory gating has been largely investigated in schizophrenia (Micoulaud Franchi, Vion Dury, & Cermolacce, 2013) but very few investigated in ADHD.

A sensory gating deficit can be assessed with auditory eventrelated potentials (ERP) (Freedman et al., 1987) and with a self-report questionnaire (the Sensory Gating Inventory, SGI) (Hetrick, Erickson, & Smith, 2012). Auditory ERP measure the suppression of the P50 component (a middle latency positive ERP component occurring approximately 50 ms after the onset of a brief auditory stimulus) in a dual-click conditioning-testing paradigm (Freedman et al., 1987). P50 suppression refers to the decrement of the P50 amplitude after the second stimulus (testing stimulus, S2) versus the P50 amplitude after the first stimulus (conditioning stimulus, S1) (Adler et al., 1982). The decrement of the P50 amplitude is considered as a neurophysiological measure of the ability to filter intrusive sensory information (Light & Braff, 2003). The SGI is composed of 36 items addressing a broad range of subjective daily perceptual experiences related to sensory gating. The psychometric properties of the SGI indicate that it provides valuable information on four dimensions of perceptual anomalies: Perceptual Modulation (PM; linked to 16 items, e.g., "My hearing is so sensitive that ordinary sounds become uncomfortable"), Over-Inclusion (OI; 7 items, e.g., "I notice background noises more than other people"), Distractibility (D; 8 items, e.g., "There are times when I can't concentrate with even the slightest sounds going on"), and Fatigue-Stress Modulation (FS; 5 items, e.g., "It seems that sounds are more intense when I'm stressed") (Hetrick et al., 2012; Micoulaud-Franchi et al.,

Many studies on schizophrenia have identified a P50 suppression deficit (Adler et al., 1982; Clementz, Geyer, & Braff, 1997). Patients with schizophrenia scored higher than healthy subjects did on the SGI and report being flooded with sensory stimuli (Micoulaud-Franchi et al., 2014a). In addition, patients with high P50 suppression deficits report the most perceptual abnormal experiences (Micoulaud-Franchi et al., 2014a). These data confirm an inability to control the sensitivity to sensory stimuli in schizophrenia (McGhie & Chapman, 1961; Venables, 1964). Thus, a sensory gating deficit can be considered a core psychophysiological deficit in schizophrenia (de Wilde, Bour, Dingemans, Koelman, & Linszen, 2007), with a relationship between abnormal neurophysiological (ERP) and clinical (SGI) features of sensory gating (Micoulaud-Franchi et al., 2014a).

Few studies investigated sensory gating deficit in adults with ADHD. Only two studies investigated P50 suppression (Holstein et al., 2013; Olincy et al., 2000). Olincy et al. (2000) were the first to investigate P50 suppression in adults with ADHD compared to healthy subjects and reported no significant differences. The authors suggested that the lack of significance may have be due to the small sample size of the their study (16 adults with ADHD) (Olincy et al., 2000). Holstein et al. (2013) investigated P50 suppression in 26 adults with ADHD and reported a significant P50 suppression deficit compared to healthy subjects. The same result was found in 22 children and adolescents with ADHD (Durukan

et al., 2011). These contradictory studies highlight the need for further investigations of P50 suppression in adults with ADHD. Only one study investigated the abnormal perceptual experience of being flooded with sensory stimuli in adults with ADHD (Sable et al., 2012). Using a short version of the SGI (17 items), Sable et al. (2012) confirmed that adults with ADHD (22 subjects) reported higher scores in the SGI than healthy subjects, particularly on the Distractibility dimension. However, the short version of the SGI did not investigate the Fatigue-Stress Modulation dimension that could be important in ADHD because of the role of fatigue (Yoon, Jain, & Shapiro, 2013), stress (Purper-Ouakil, Wohl, Michel, Mouren, & Gorwood, 2004) and vigilance alterations (Hegerl & Hensch, 2014; Philip et al., 2005). Finally, to the best of our knowledge, no study investigated both P50 suppression and abnormal perceptual experiences with all 36 items of the SGI in adults with ADHD, as has been performed with patients with schizophrenia (Micoulaud-Franchi et al., 2014a). Thus, the relationships between abnormal neurophysiological (ERP) and clinical (SGI) features of sensory gating need to be investigated in adults with ADHD.

Therefore, the aim of the present study was to investigate both P50 suppression and SGI scores in adults with ADHD compared to patients with schizophrenia and healthy subjects to get a better understanding of sensory gating deficit in adults with ADHD (Johannesen, Bodkins, O'Donnell, Shekhar, & Hetrick, 2008; Kisley, Noecker, & Guinther, 2004). The primary hypotheses were that adults with ADHD in comparison with healthy subjects: (i) would exhibit P50 suppression deficit (Holstein et al., 2013) and (ii) would report higher overall SGI scores (Sable et al., 2012). The secondary hypotheses were that adults with ADHD in comparison with patients with schizophrenia: (i) would report more abnormal perceptual experiences on the Distractibility dimension (Sable et al., 2012) and the Fatigue-Stress dimension of the SGI, in line with the core inattention symptom in ADHD (American Psychiatric Association, 2000) and the role of fatigue and stress in this disorder (Purper-Ouakil et al., 2004; Yoon et al., 2013), and (ii) would exhibit the same relationship found between P50 suppression deficit and SGI scores (Micoulaud-Franchi et al., 2014a).

2. Methods and materials

2.1. Participants

Twenty-four adult patients with ADHD (30.2 \pm 7.9 years, female: 8) were recruited from the Department of Psychiatry, Marseille University Hospital, France. Comparison subjects were 24 outpatients with chronic and clinically stable schizophrenia (31.3 \pm 10.8 years, female: 8) and 24 healthy subjects $(36.5 \pm 11.2 \text{ years},$ female: 8). Patients with ADHD were diagnosed by a psychiatrist according to the Conners adult ADHD diagnostic interview for DSM-IV-TR (CAADID) (Conners, Epstein, & Johnson, 2001). Patients with schizophrenia were diagnosed by a psychiatrist according to the Structured Clinical Interview for DSM-IV interviews (SCID) (American Psychiatric Association, 2000; First, Gibbon, & Williams, 1997). Healthy subjects were not taking any psychotropic medications and were screened for any current or lifetime history of a DSM-IV axis I disorder, using the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) and for any current or lifetime history of ADHD based on the CAADID (Conners et al., 2001). We ensured that healthy subjects had no affected family members with ADHD, schizophrenia or bipolar disorder (Gottesman & Gould, 2003). We ensured that adults with ADHD, patients with schizophrenia and healthy subjects were similar in age, sex, and educational level. Exclusion criteria were reduced capacity to consent, mental retardation, auditory impairment, current depression, current or lifetime history of bipolar disorder, current anxiety disorder, drug or alcohol addiction, neurological illness, brain injury or severe medical disorders.

After receiving a detailed description of the study, participants gave their written informed consent. This study was conducted in accordance with the Declaration of Helsinki and French Good Clinical Practices. The data collection was approved by the *Commission nationale de l'informatique et des libertés* (CNIL number: 1223715).

2.2. Clinical measures

The Adult ADHD Self-Report Scale (ASRS) assessed the clinical severity of patients with ADHD (Kessler et al., 2005; Morin, Tran, & Caci, 2013). This scale consists of 18 items reflecting the DSM-IV-TR diagnostic criteria and rated from 0="never" to 4="very frequently". Scores were computed from the ASRS for an inattention factor and a hyperactivity factor.

The Positive and Negative Syndrome Scale (PANSS) assessed the clinical severity of patients with schizophrenia (Kay, Fiszbein, & Opler, 1987). Scores were computed from the PANSS for a positive symptom, negative symptom, excited, depressive and cognitive factors (Lancon, Aghababian, Llorca, & Auquier, 1998).

The Trait Anxiety Inventory (TAI) was administered to all participants in each group to investigate anxiety symptoms (Spielberger & Vagg, 1984).

The number of adults with ADHD medicated with methylphenidate was collected (none of the patients were medicated with other molecular formula). The mean methylphenidate dose was calculated for this population. All patients with schizophrenia were medicated with typical or atypical neuroleptics. In this population, the mean chlorpromazine equivalent dose was calculated (Davis, 1976; Woods, 2003).

2.3. P50 suppression measurement

Subjects were recorded seated in a comfortable recliner in a quiet room, wore headphones for the auditory stimuli presentation and were instructed to stay awake, relaxed and to keep their eyes closed. Subjects were asked to abstain from cigarette smoking for 1 h before the electrophysiological measurements (Adler, Hoffer, Wiser, & Freedman, 1993). During the recording, the participants were monitored visually and by EEG for signs of drowsiness or sleep; if either occurred, the technician neurophysiologist briefly spoke to and aroused the participant (Yee et al., 2010).

Electroencephalographic activity (EEG) was recorded from a scalp gold disc electrode affixed to the vertex (Cz) according to the International 10/20 convention. The ground electrode was on the nose and the reference electrode was on an ear. Electrode resistance was less than $10\,\mathrm{k}\Omega$. Data were acquired at a $1000\,\mathrm{Hz}$ sampling frequency and filtered with a band pass filter of 1–200 Hz to reduce the noise in the EEG (de Wilde et al., 2007). Data were segmented into single trials of 1200 ms, beginning 200 ms before the S1 stimulus onset. Electro-oculographic data were recorded, and trials contaminated by ocular movements and movement artifacts were rejected by visual inspection. The remaining trials were averaged for each participant

Auditory stimuli were delivered in a *conditioning-testing P50* paradigm consisting of a click pair presentation (conditioning click, S1, followed by the testing click, S2) in a passive task. The interstimulus interval was set to 500 ms and the inter-pair interval to 10 s. Clicks were rectangular pulses of .05 ms with an intensity of 100 dB SPL (Baker et al., 1987; Jin et al., 1998). A set of 60 click pairs was delivered, large enough to generate robust results to extract the signal from the noise with a reasonable duration of EEG recording (around 10 min).

The conditioning P50 component was identified as the positive component presenting the largest peak occurring between 40 and 80 ms after the S1 onset (Cardenas, Gerson, & Fein, 1993; Nagamoto, Adler, Waldo, & Freedman, 1989). The testing P50 component was identified in a similar way after the S2 onset. The amplitudes of these components were defined as peak-to-peak amplitudes, *i.e.*, between the peak of the P50 component and the preceding negative peak (Boutros & Belger, 1999; Clementz et al., 1997; Nagamoto, Adler, Waldo, Griffith, & Freedman, 1991). Finally, the percentage of P50 suppression (P50_{supp}) was calculated using the following formula: P50_{supp} = $[1 - (A_{S2}/A_{S1})] \times 100$, where A_{S1} and A_{S2} are the amplitude of the conditioning and testing of the P50 component, respectively (Clementz et al., 1997). Minimums of 100% suppression or 100% facilitation were used to prevent outliers from disproportionately affecting the group means (Cadenhead, Light, Geyer, & Braff, 2000; Nagamoto et al., 1991).

2.4. The sensory gating inventory

The participants scored the 36 items of the SGI on 6-point Likert ratings (from 0 = "never true" to 5 = "always true") (Hetrick et al., 2012), which were translated and validated in French (Micoulaud-Franchi et al., 2014b). The algebraic sum of the Likert rating for each participant was computed for the overall SGI score and each of the four dimensions (Perceptual Modulation, Over-Inclusion, Distractibility and Fatigue-Stress Modulation). For each dimension scale, internal consistency reliability was assessed by Cronbach's alpha coefficient in order to confirm the consistency of the SGI in previous validation studies in large groups of healthy subjects (n = 363) (Micoulaud-Franchi et al., 2014b), of patients with ADHD (n=70) and with schizophrenia (n=70) (Micoulaud Franchi et al., Submitted). All coefficients were higher than .7 (in healthy subjects: alpha PM = .92, alpha OI = .87, alpha D = .88 and alpha FS = .79, in ADHD: alpha PM=.92, alpha OI=.87, alpha D=.89 and alpha FS = .70, and in schizophrenia: alpha PM = .95, alpha OI = .97, alpha D=.92 and alpha FS=.84), which indicated satisfactory internal consistency (Carey & Seibert, 1993; Cronbach & Meehl, 1955).

2.5. Statistical analysis

Descriptive statistics of the sample included frequencies and percentages of categorical variables, together with means and standard deviations of continuous variables. Neurophysiological data were square root transformed to approximate the normal distributional assumptions required by parametric statistical methods. Data analyses were performed using SPSS software (Version 18, PASW Statistics) and Prism software (Version 6, GraphPad).

To determine if adults with ADHD exhibited P50 suppression deficit and reported higher SGI scores (overall scores and scores for each of the four dimensions) than healthy subjects or patients with schizophrenia, overall effects between the three groups were compared using analysis of variance (single-factor ANOVA with F-test statistics). Tukey's tests were used to correct *post-hoc* multiple comparisons and to determine which groups significantly differed from each other.

To examine the relationship between P50 suppression and SGI scores (overall and the four dimensions), Pearson correlation coefficients were computed for each of the three groups. For adults with ADHD, Pearson correlation coefficients were also computed between the ASRS scores (overall, inattention and hyperactivity) and both the P50 suppression and SGI scores (overall and the four dimensions). For patients with schizophrenia, Pearson correlation coefficients were also computed between the PANSS scores (overall and the five factor scores) and both the P50 suppression and SGI scores (overall and the four dimensions).

Age and Education level were compared using ANOVA and Tukey's *post-hoc* tests. Sex was analyzed using χ^2 tests.

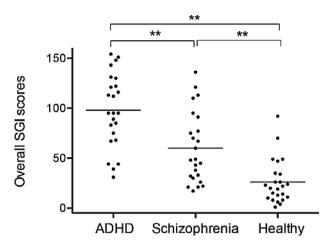


Fig. 1. Overall SGI scores for adults with ADHD, patients with schizophrenia and healthy subjects. Mean (bar) and individual values are shown.

For each analysis, effects were considered as significant when the *P*-value was equal to or less than .05.

3. Results

Table 1 shows the demographic data, P50 parameters and SGI scores.

Age, Sex and Educational Level were not significantly different between the three groups.

The mean ASRS overall score for adults with ADHD was 51.62 (SD=8.07), ASRS inattention score was 28.25 (SD=4.54) and ASRS hyperactivity score was 23.37 (SD=6.21). Eight patients (33%) were medicated with methylphenidate. The mean dose was $31.5 \, \text{mg}$ (SD=8.33).

The PANSS overall score for the patients with schizophrenia was 76.6 (SD = 21.3), the positive symptom factor was 14.8 (SD = 6.5), the negative symptom factor was 20.7 (SD = 6.8), the excited factor was 10.5 (SD = 3.2), the depressive factor was 10.5 (SD = 3.9) and the cognitive factor was 18.7 (SD = 6.8). The mean chlorpromazine dose was 512.4 mg (SD = 437.9).

Adults with ADHD reported higher overall SGI scores (Fig. 1) and higher scores for each of the four dimensions than the healthy subjects and patients with schizophrenia (Table 1). Patients with schizophrenia reported higher overall SGI scores and higher scores for the dimensions of the SGI than healthy subjects, except the Fatigue–Stress Modulation dimension despite a trend (p = .056).

Adults with ADHD and patients with schizophrenia exhibited a significant P50 suppression deficit compared to healthy subjects (Fig. 2). There was no difference between adults with ADHD and patients with schizophrenia (P=.68)

For adults with ADHD, the Pearson correlation coefficients with P50 suppression were significant for overall SGI scores $(r(24)=-.655,\ P=.001)$ (Fig. 3) and for the four dimensions: Perceptual Modulation $(r(24)=-.615,\ P=.001)$, Over-Inclusion $(r(24)=-.512,\ P=.011)$, Distractibility $(r(24)=-.628,\ P=.001)$ and Fatigue–Stress Modulation $(r(24)=-.708,\ P<.0001)$. Adults with ADHD with sensory gating deficit report more perceptual abnormalities than patients without sensory gating deficit (Fig. 4).

For patients with schizophrenia, the Pearson correlation coefficients with P50 suppression were significant for overall SGI scores (r(24) = -.499, P = .013) and two dimensions: Over-Inclusion scores (r(24) = -.527, P = .008) and Distractibility scores (r(24) = -.535, P = .007). Trends were found for Perceptual modulation scores (r(24) = -.354, P = .09) and Fatigue–Stress Modulation scores (r(24) = -.381, P = .06). For healthy subjects, the Pearson

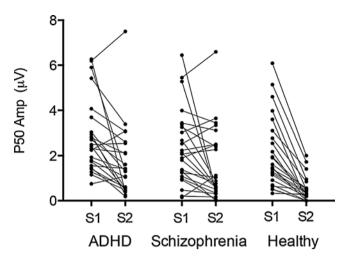


Fig. 2. Amplitudes of the conditioning (S1) and testing (S2) P50 component for adults with ADHD, patients with schizophrenia and healthy subjects.

correlation coefficients between SGI scores and P50 suppression were not significant.

Pearson correlation coefficients between the ASRS scores and the P50 suppression for adults with ADHD and between the PANSS scores and the P50 suppression for patients with schizophrenia were not significant. Pearson correlation coefficients between the ASRS inattention scores and the SGI scores for adults with ADHD were significant: overall SGI score (r(24) = -.482, P = .017), Perceptual Modulation scores (r(24) = -.405, P = .049), Over-Inclusion scores (r(24) = -.468, P = .021), Distractibility scores (r(24) = -.533, P = .007) and Fatigue–Stress Modulation scores (r(24) = -.442, P = .03). Pearson correlation coefficient between the PANSS scores and the SGI scores for adults with schizophrenia were not significant.

4. Discussion

To our knowledge, this is the first study that investigated both P50 suppression and abnormal perceptual experiences related to sensory gating within the same group of adults with ADHD.

Concerning P50 suppression, the main result of the present study was that adults with ADHD exhibited a significant P50 suppression deficit in a dual click conditioning-testing paradigm compared to healthy subjects, as did patients with schizophrenia. This finding indicates the inability to filter intrusive sensory information in adults with ADHD. Previous studies with eventrelated potentials (ERP) confirmed attentional dysfunction in ADHD (Itagaki et al., 2011), the present ERP study suggests that a elementary form of pre-attentive information processing is also altered in ADHD (Braff & Geyer, 1990). This finding is in line with Holstein et al. (2013), in contrast to the results of Olincy et al. (2000). As suggested by Holstein et al. (2013), the lack of significance in the Olincy et al. study could be related to their small sample size (16, compared to 24 in the present study) and the use of a small number of stimuli (48, compared to 60 in the present study) and relatively low stimulus intensity (70 dB, compared to 100 dB in the present study). Moreover, as in this previous study, the reduced sensory gating was due to the difference in the amplitude elicited by S2 rather than S1 (Olincy et al., 2000). In patients with schizophrenia, the significant P50 suppression deficit is consistent with many previous studies (de Wilde et al., 2007; Patterson et al., 2008).

Concerning abnormal perceptual experiences, the main result of the present study is that adults with ADHD reported significantly higher SGI scores (overall and for each of the four dimensions) than healthy subjects. This finding confirms the abnormal perceptual

Table 1Demographic, demographic data, P50 parameters and SGI scores the three groups: adults with ADHD, patients with schizophrenia (SCZ), and healthy subjects (HLT).

	ADHD		Schizophrenia		Healthy subjects		Significance		Pairwise ^b
	Mean	SD	Mean	SD	Mean	SD	F	P	
Sex (number of subjects)									
Male	16	_	16	_	16	_	_	_	_
Female	8	-	8		8	-		-	-
Age (years)	30.25	7.92	31.33	10.84	36.54	11.19	2.66	.07	_
Education level (years)	13.29	3.02	13.16	2.91	12.29	3.71	.68	.51	_
Stimulus S1									
P50 amplitude (μV)	2.85	1.62	2.38	1.66	2.07	1.64	1.35	.26	_
P50 latency (ms)	57.83	14.99	58.25	14.72	63.01	9.39	1.12	.33	-
Stimulus S2									
P50 amplitude (μV)	1.65	1.58	1.57	1.61	.43	.58	6.11	.004	ADHD = SCZ > HLT
P50 latency (ms)	55.52	14.45	59.25	14.84	62.95	10.84	1.81	.17	_
P50-suppression ^a (%)	39.48	39.43	29.92	51.08	76.56	23.25	9.28	<.001	ADHD = SCZ > HLT
TAI	46.43	6.56	38.66	13.71	27.37	6.17	24.56	<.001	ADHD > SCZ > HLT
SGI									
Overall score	97.95	36.78	60.01	35.39	26.08	21.98	30.12	<.001	ADHD > SCZ > HLT
Perceptual modulation	34.75	18.43	22.01	16.16	7.37	9.43	19.58	<.001	ADHD > SCZ > HLT
Over-inclusion	20.33	9.12	12.58	8.54	5.37	5.62	21.45	<.001	ADHD > SCZ > HLT
Distractibility	30.12	6.61	16.91	9.61	8.33	6.67	48.02	<.001	ADHD > SCZ > HLT
Fatigue-Stress modulation	12.75	5.57	8.5	6.06	5.00	3.49	13.57	<.001	ADHD > SCZ = HLT

^a The percentage of P50 suppression was calculated as $[1 - (stimulus 2 amplitude/stimulus 1 amplitude)] <math>\times$ 100.

experience of being flooded with sensory stimuli in adults with ADHD and replicates the results of Sable et al. (2012). However, this previous study found a significant result only for the Distractibility dimension of the SGI. The lack of difference concerning Perceptual Modulation and Over-inclusion dimensions could be due to the use

of a short version of the SGI (17 versus 36 items) (Sable et al., 2012) that may be a less accurate manner of assessing abnormal perceptual experience than the original version used in the present study. A second explanation could be higher clinical severity of ADHD (mean ASRS > 30) in our study compared to the study of Sable

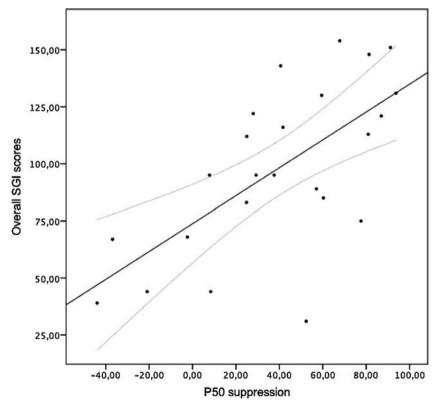


Fig. 3. Correlation between P50 suppression and overall SGI scores in 24 adults with ADHD.

b Tukey's *post-hoc* pairwise comparisons: >: *P* < 0.05.

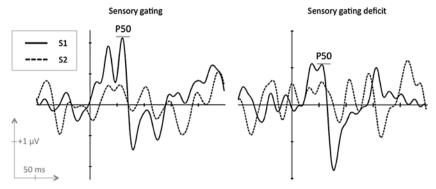


Fig. 4. P50 component waveforms for S1 (conditioning stimulus, solid line) and S2 (testing stimulus, dotted line) for one patient with ADHD with no sensory gating deficit and no abnormal perceptual experience reported to the SGI (left) and for one patient with ADHD with sensory gating deficit and high score at the SGI, corresponding to the experience of being flooded by external stimuli (right). The data of each subject were epoched from 100 ms preceding (baseline) to 250 ms following S1 and S2 onsets and corrected for baseline activity. Prior to averaging, signals were filtered between 5 and 47-Hz to optimize the waveform of the P50 component.

et al. (2012). Indeed, we found a relationship between the clinical symptom of inattention (as reported in the ASRS) and abnormal perceptual experience (as reported in the SGI). Although the clinical severity of ADHD was not investigated in the study of Sable et al. (2012), the different method of recruitment between that and the present study (email sent to students in psychology courses in the first case versus consultation in a specialized Department of psychiatry in our study) is in favor of different clinical severity between the ADHD groups of these two studies.

The secondary result, concerning abnormal perceptual experience, was that adults with ADHD reported higher SGI scores than patients with schizophrenia. As we hypothesized, adults with ADHD reported higher scores on the Distractibility and the Fatigue-Stress Modulation dimensions consistent with the role of fatigue and stress in the pathophysiology of inattention in ADHD (Biederman, 2005; Faraone et al., 2000; Hegerl & Hensch, 2014; Purper-Ouakil et al., 2004; Yoon et al., 2013). Compared to healthy subjects, Fatigue-Stress Modulation scores were higher for adults with ADHD, but not for patients with schizophrenia. This difference could indicate a perceptual vulnerability during periods of fatigue and stress more specific to ADHD than schizophrenia. In contrast to our hypotheses, Perceptual Modulation and Over-Inclusion dimensions were also higher in adults with ADHD compared to patients with schizophrenia. Although the SGI was developed for schizophrenia (Hetrick et al., 2012), this result highlights the ability of this scale to investigate clinical features of ADHD and could indicate higher abnormal perceptual experience in ADHD than found in patients with schizophrenia. However, a second explanation could be that adults with ADHD, compared to patients with schizophrenia, are better able to report their abnormal perceptual experience (Jin et al., 1998; Light & Braff, 2000).

Concerning the relationship between P50 suppression deficit and abnormal perceptual experience, the current results replicated the relationship between neurophysiological and clinical features of sensory gating in schizophrenia found in a recent study (Micoulaud-Franchi et al., 2014a), which confirmed our hypothesis that the same psychophysiological relationship would be found in adults with ADHD. As to patients with schizophrenia, it may indicate that abnormal neurophysiologic responses to repetitive stimuli in ADHD give rise to clinically relevant perceptions of being flooded with sensory stimuli.

Some limitations of the current study warrant consideration. First, the sample size is quite small and, therefore, might not be representative. Although the sample size is larger than the sample in Olincy et al. (2000) study and similar to the Holstein et al. (2013) study, our results need to be replicated using a larger cohort of

adults with ADHD. A larger cohort may also allow the investigation of potential sensory gating differences between ADHD subtypes. Second, although, 33% of our sample taking stimulant medication, we don't think this would have influenced the results because a supplementary analysis in our study found no significant difference in ASRS scores, SGI scores and P50 suppression between ADHD medicated and non-medicated adults with ADHD. Third, a washout period of 48 h for medication was not carried out. In schizophrenia, the relationship between P50 suppression and perpetual abnormalities related to sensory gating was found in medicated patients (Micoulaud-Franchi et al., 2014a). Moreover, in schizophrenia it has been suggested "the accuracy of self-reports of deficits or gating experiences <would> be compromised when patients are unmedicated" (Light & Braff, 2000). Thus, we have decided to not washout patients with ADHD. However, medication could modify the relation between neurophysiological and clinical features of sensory gating (Micoulaud Franchi et al., in press). Thus, longitudinal studies measuring P50 suppression, SGI scores and their relationship, before and during treatment with methylphenidate, need to be conducted. Four, the use of a self-rating subjective scale (ASRS) to measure the severity of ADHD could be criticized. However, the ASRS has a satisfactory convergent validity with the Conners Adult Attention-Deficit/Hyperactivity Disorder Rating Scale (CAARS) (Spencer et al., 2009), which was rated by the investigator (Conners, Erhardt, & Sparrow, 1999). Five, adults with ADHD and patients with schizophrenia exhibited a significant higher state anxiety scores compared to healthy subjects. As anxiety appears to be a possible contributor to a deficit in P50 suppression (White, Kanazawa, & Yee, 2005; White & Yee, 1997), it could be a confounding factor in the present results. However, we did not find significant correlations between the TAI scores and P50 suppression or SGI scores in any of the three groups.

In conclusion, the present study provides information leading to a better understanding of sensory gating deficit in adults with ADHD. Sensory gating deficit can be considered a core psychophysiological deficit in ADHD, with a relationship between abnormal neurophysiological (ERP) and clinical (SGI) features of sensory gating. Further investigations should analyzed protective effect of sensory gating on higher cognitive function in ADHD (Venables, 1964). In particular, the relationship between ERP related to attentional function, like the P300 (Itagaki et al., 2011), and P50 suppression may help to better understand the link between cognitive dysfunctions, abnormal perceptual experiences and alteration of pre-attentive information processing in ADHD. The effect of fatigue and stress, but also of stimulation medication, on this relationship should be also investigated in ADHD.

Conflict of interest statement

The authors declare no conflicts of interest.

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References

- Adler, L. E., Hoffer, L. D., Wiser, A., & Freedman, R. (1993). Normalization of auditory physiology by cigarette smoking in schizophrenic patients. *The American Journal* of Psychiatry, 150, 1856–1861.
- Adler, L. E., Pachtman, E., Franks, R. D., Pecevich, M., Waldo, M. C., & Freedman, R. (1982). Neurophysiological evidence for a defect in neuronal mechanisms involved in sensory gating in schizophrenia. *Biological Psychiatry*, 17, 639–654.
- American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorder (4th ed, Text Revision (DSM-IV-TR)). Washington, DC: American Psychiatric Association.
- Baker, N., Adler, L. E., Franks, R. D., Waldo, M., Berry, S., Nagamoto, H., et al. (1987). Neurophysiological assessment of sensory gating in psychiatric inpatients: Comparison between schizophrenia and other diagnoses. *Biological Psychiatry*, 22, 603–617
- Biederman, J. (2005). Attention-deficit/hyperactivity disorder: A selective overview. Biological Psychiatry, 57, 1215–1220.
- Boutros, N. N., & Belger, A. (1999). Midlatency evoked potentials attenuation and augmentation reflect different aspects of sensory gating. *Biological Psychiatry*, 45, 917–922.
- Braff, D. L., & Geyer, M. A. (1990). Sensorimotor gating and schizophrenia. Human and animal model studies. Archives of General Psychiatry, 47, 181–188.
- Caci, H. M., Morin, A. J., & Tran, A. (2014). Prevalence and correlates of attention deficit hyperactivity disorder in adults from a French community sample. The Journal of Nervous and Mental Disease, 202, 324–332.
- Cadenhead, K. S., Light, G. A., Geyer, M. A., & Braff, D. L. (2000). Sensory gating deficits assessed by the P50 event-related potential in subjects with schizotypal personality disorder. The American Journal of Psychiatry, 157, 55–59.
- Cardenas, V. A., Gerson, J., & Fein, G. (1993). The reliability of P50 suppression as measured by the conditioning/testing ratio is vastly improved by dipole modeling. *Biological Psychiatry*, 33, 335–344.
- Carey, R. G., & Seibert, J. H. (1993). A patient survey system to measure quality improvement: Questionnaire reliability and validity. Medical Care, 31, 834–845.
- Clementz, B. A., Geyer, M. A., & Braff, D. L. (1997). P50 suppression among schizophrenia and normal comparison subjects: A methodological analysis. *Biological Psychiatry*, 41, 1035–1044.
- Conners, C., Epstein, J., & Johnson, D. (2001). Conner's adult ADHD diagonostic interview for DSM-IV: CAADID: Technical manual, Torronto: MHS.
- Conners, C., Erhardt, D., & Sparrow, W. (1999). Conners' adult ADHD rating scales (CAARS) technical manual. New York, NY: Multi-Health Systems.
- Cronbach, L. J., & Meehl, P. E. (1955). Construct validity in psychological tests. Psychological Bulletin, 52, 281–302.
- chological Bulletin, 52, 281–302.

 Davis, J. M. (1976). Comparative doses and costs of antipsychotic medication. Archives of General Psychiatry, 33, 858–861.
- de Wilde, O. M., Bour, L. J., Dingemans, P. M., Koelman, J. H., & Linszen, D. H. (2007). A meta-analysis of P50 studies in patients with schizophrenia and relatives: Differences in methodology between research groups. Schizophrenia Research, 97. 137–151.
- Durukan, I., Yucel, M., Erdem, M., Kara, K., Oz, O., Karaman, D., et al. (2011). P50 sensory gating in children and adolescents with ADHD and effects of methylphenidate administration on P50 sensory gating. Bulletin of Clinical Psychopharmacology, 21, 42–48.
- Faraone, S. V., Biederman, J., Spencer, T., Wilens, T., Seidman, L. J., Mick, E., et al. (2000). Attention-deficit/hyperactivity disorder in adults: An overview. *Biological Psychiatry*, 48, 9–20.
- Fayyad, J., De Graaf, R., Kessler, R., Alonso, J., Angermeyer, M., Demyttenaere, K., et al. (2007). Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. *The British Journal of Psychiatry*, 190, 402–409.
- First, R., Gibbon, M., & Williams, J. (1997). Structured clinical interview for DSM-IV axis I disorders: Clinical version (SCID-CV). Washington, DC: American Psychiatric Press.
- Freedman, R., Adler, L. E., Gerhardt, G. A., Waldo, M., Baker, N., Rose, G. M., et al. (1987). Neurobiological studies of sensory gating in schizophrenia. *Schizophrenia Bulletin*, 13, 669–678.
- Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. The American Journal of Psychiatry, 160, 636–645.
- Hegerl, U., & Hensch, T. (2014). The vigilance regulation model of affective disorders and ADHD. Neuroscience & Biobehavioral Reviews, 44C, 45–57.
- Hetrick, W. P., Erickson, M. A., & Smith, D. A. (2012). Phenomenological dimensions of sensory gating. Schizophrenia Bulletin, 38, 178–191.

- Holstein, D. H., Vollenweider, F. X., Geyer, M. A., Csomor, P. A., Belser, N., & Eich, D. (2013). Sensory and sensorimotor gating in adult attention-deficit/hyperactivity disorder (ADHD). Psychiatry Research, 205, 117–126.
- Hudziak, J. J., Althoff, R. R., Derks, E. M., Faraone, S. V., & Boomsma, D. I. (2005). Prevalence and genetic architecture of Child Behavior Checklist-juvenile bipolar disorder. *Biological Psychiatry*, 58, 562–568.
- Itagaki, S., Yabe, H., Mori, Y., Ishikawa, H., Takanashi, Y., & Niwa, S. (2011). Event-related potentials in patients with adult attention-deficit/hyperactivity disorder versus schizophrenia. Psychiatry Research, 189, 288–291.
- Jin, Y., Bunney, W. E., Jr., Sandman, C. A., Patterson, J. V., Fleming, K., Moenter, J. R., et al. (1998). Is P50 suppression a measure of sensory gating in schizophrenia? *Biological Psychiatry*, 43, 873–878.
- Johannesen, J. K., Bodkins, M., O'Donnell, B. F., Shekhar, A., & Hetrick, W. P. (2008). Perceptual anomalies in schizophrenia co-occur with selective impairments in the gamma frequency component of midlatency auditory ERPs. *Journal of Abnor*mal Psychology, 117, 106–118.
- Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophrenia Bulletin, 13, 261–276.
- Kessler, R. C., Adler, L., Ames, M., Demler, O., Faraone, S., Hiripi, E., et al. (2005). The World Health Organization Adult ADHD Self-Report Scale (ASRS): A short screening scale for use in the general population. *Psychological Medicine*, 35, 245–256.
- Kisley, M. A., Noecker, T. L., & Guinther, P. M. (2004). Comparison of sensory gating to mismatch negativity and self-reported perceptual phenomena in healthy adults. *Psychophysiology*, 41, 604–612.
- Lancon, C., Aghababian, V., Llorca, P. M., & Auquier, P. (1998). Factorial structure of the Positive and Negative Syndrome Scale (PANSS): A forced five-dimensional factor analysis. Acta Psychiatrica Scandinavica, 98, 369–376.
- Light, G. A., & Braff, D. (2003). Sensory gating deficits in schizophrenia: Can we parse the effects of medication, nicotine use, and changes in clinical status. *Clinical Neuroscience Research*, 3, 47–54.
- Light, G. A., & Braff, D. L. (2000). Do self-reports of perceptual anomalies reflect gating deficits in schizophrenia patients? *Biological Psychiatry*, 47, 463–467.
- McGhie, A., & Chapman, J. (1961). Disorders of attention and perception in early schizophrenia. *British Journal of Medical Psychology*, 34, 103–116.
- Micoulaud Franchi, J. A., Aramaki, M., Geoffroy, P., Richieri, R., Cermolacce, M., & Faget-Agius, C. et al. In press. Effects of clozapine on perceptual abnormalities and sensory gating. A preliminary cross-sectional study in schizophrenia. Journal of Clinical Psychopharmacology.
- Micoulaud Franchi, J. A., Lopez, R., Vaillant, F., Richieri, R., El-Kaim, A., & Bioulac, B. et al., Submitted. Perceptual abnormalities related to sensory gating deficit are core symptoms in adults with ADHD. Psychiatry Research.
- Micoulaud Franchi, J. A., Vion Dury, J., & Cermolacce, M. (2013). Neurophysiological endophenotypes and schizophrenic disorder: Emergence and evolution of a clinical concept. *Encephale*, 38(Suppl. 3), S103L 109.
- Micoulaud-Franchi, J. A., Hetrick, W. P., Aramaki, M., Bolbecker, A., Boyer, L., Ystad, S., et al. (2014). Do schizophrenia patients with low P50-suppression report more perceptual anomalies with the sensory gating inventory? *Schizophrenia Research*, 157, 157–162.
- Micoulaud-Franchi, J. A., Hetrick, W. P., Boyer, L., Bolbecker, A., Aramaki, M., Ystad, S., et al. (2014). Validation of the French sensory gating inventory: A confirmatory factor analysis. *Psychiatry Research*, 220, 1106–1112.
- Morin, A. J., Tran, A., & Caci, H. (2013). Factorial validity of the ADHD adult symptom rating scale in a french community sample: Results from the ChiP-ARDS study. Journal of Attention Disorders [Epub ahead of print], May 31.
- Nagamoto, H. T., Adler, L. E., Waldo, M. C., & Freedman, R. (1989). Sensory gating in schizophrenics and normal controls: Effects of changing stimulation interval. *Biological Psychiatry*, 25, 549–561.
- Nagamoto, H. T., Adler, L. E., Waldo, M. C., Griffith, J., & Freedman, R. (1991). Gating of auditory response in schizophrenics and normal controls. Effects of recording site and stimulation interval on the P50 wave. Schizophrenia Research, 4, 31–40.
- Olincy, A., Ross, R. G., Harris, J. G., Young, D. A., McAndrews, M. A., Cawthra, E., et al. (2000). The P50 auditory event-evoked potential in adult attention-deficit disorder: Comparison with schizophrenia. *Biological Psychiatry*, 47, 969–977.
- Patterson, J. V., Hetrick, W. P., Boutros, N. N., Jin, Y., Sandman, C., Stern, H., et al. (2008). P50 sensory gating ratios in schizophrenics and controls: A review and data analysis. *Psychiatry Research*, 158, 226–247.
- Philip, P., Sagaspe, P., Taillard, J., Valtat, C., Moore, N., Akerstedt, T., et al. (2005). Fatigue, sleepiness, and performance in simulated versus real driving conditions. Sleep. 28. 1511–1516.
- Purper-Ouakil, D., Wohl, M., Michel, G., Mouren, M. C., & Gorwood, P. (2004). Symptom variations in ADHD: Importance of context, development and comorbidity. *Encephale*, 30, 533–539.
- Sable, J. J., Kyle, M. R., Knopf, K. L., Schully, L. T., Brooks, M. M., Parry, K. H., et al. (2012). The Sensory Gating Inventory as a potential diagnostic tool for attention-deficit hyperactivity disorder. Attention Deficit and Hyperactivity Disorders, 4, 141–144.
- Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., et al. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry*, 59(Suppl. 20), 22–33 (quiz 34–57).
- Spencer, T. J., Adler, L. A., Meihua, Q., Saylor, K. E., Brown, T. E., Holdnack, J. A., et al. (2009). Validation of the adult ADHD investigator symptom rating scale (AISRS). *Journal of Attention Disorders*, 14, 57–68.
- Spielberger, C. D., & Vagg, P. R. (1984). Psychometric properties of the STAI: A reply to Ramanaiah, Franzen, and Schill. *Journal of Personality Assessment*, 48, 95–97.

- Venables, P. H. (1964). Input dysfunction in schizophrenia. Progress in Experimental Personality Research, 72, 1-47.
- White, P. M., Kanazawa, A., & Yee, C. M. (2005). Gender and suppression of mid-latency ERP components during stress. *Psychophysiology*, 42, 720–725.
- White, P. M., & Yee, C. M. (1997). Effects of attentional and stressor manipulations on the P50 gating response. *Psychophysiology*, 34, 703–711. Woods, S. W. (2003). Chlorpromazine equivalent doses for the newer atypical
- antipsychotics. Journal of Clinical Psychiatry, 64, 663-667.
- Yee, C. M., Williams, T. J., White, P. M., Nuechterlein, K. H., Ames, D., & Subotnik, K. L. (2010). Attentional modulation of the P50 suppression deficit in recent-onset and chronic schizophrenia. Journal of Abnormal Psychology, 119,
- Yoon, S. Y., Jain, U. R., & Shapiro, C. M. (2013). Sleep and daytime function in adults with attention-deficit/hyperactivity disorder: Subtype differences. Sleep Medicine, 14, 648-655.