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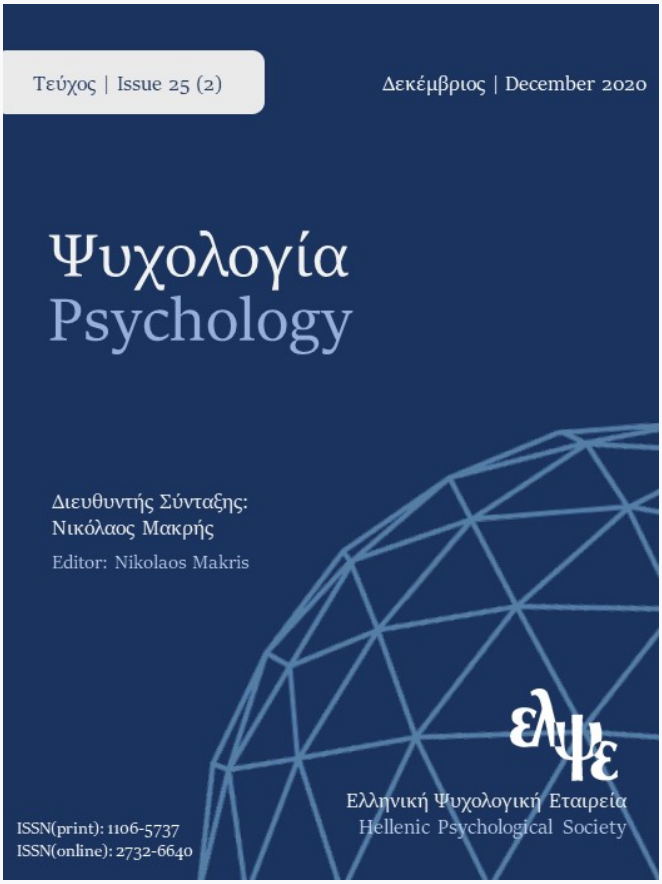

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ΕΜΠΕΙΡΙΚΗ ΕΡΓΑΣΙΑ | RESEARCH PAPER

Associations of multidimensional temperament and character profiles with cognition and sensorimotor gating in individuals at risk for schizophrenia-spectrum disorders: preliminary findings

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KEYWORDS

cognition,
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ABSTRACT

Cloninger's biopsychological model for personality distinguishes between Temperament [Novelty Seeking, Harm Avoidance (HA), Reward Dependence (RD), Persistence (PS)], and Character [Self-Directedness (SD), Cooperativeness (CO), Self-Transcendence (ST)] traits. Cloninger has also described three sets of complex interactions among these traits, which can be summarized as a linked network of three cubes. Within each cube, the different combinations of the sub-dimensions formulate multidimensional profiles that describe personality more accurately compared with their individual constituents. The aim of the present study was to examine differences of these multidimensional profiles in cognitive functions and Prepulse Inhibition (PPI) in unaffected relatives of schizophrenia-spectrum patients and control individuals**.** We assessed 114 unaffected relatives of schizophrenia-spectrum patients and 122 controls for Temperament/Character traits, a wide range of cognitive functions, and PPI of the acoustic startle reflex. The relatives had higher Harm Avoidance and Self-Transcendence along with lower Reward Dependence, Persistence, Self-Directedness and Cooperativeness scores as well as lower PPI and poorer cognition compared with controls. We also found a) unequal distribution of relatives and controls in several "disadvantageous" profiles associated with the schizophrenia-spectrum, b) the Schizotypal/Disorganized, Apathetic and Fragile profiles had poorer emotional decision making and attention switching, respectively, compared with their "advantageous" counterparts and c) the Adventurous, Independent, Bossy and Resilient profiles had higher PPI compared with their counterparts. These findings further highlight the significance of personality determinants of cognitive processes and have potential implications in early intervention programs in the schizophrenia-spectrum.

Cloninger's biopsychological model for personality (Cloninger et al., 1993) distinguishes between Temperament and Character higher-order dimensions. Temperament describes individual differences in percept-based habits and skills (Cloninger, 1994) and comprises four independently inherited sub-dimensions that remain moderately stable throughout life (Cloninger & Svrakic, 1997): Novelty Seeking (NS; tendency towards exploratory activities in response to novelty), Harm Avoidance (HA; pessimistic worrying in anticipation of problems), Reward Dependence (RD; tendency to maintain behaviours in response to reward by others) and Persistence (PS; an independent dimension that refers to a tendency to perseverance despite frustration and fatigue). Character refers to individual differences in concept-based goals and values (Cloninger, 1994) and is measured by three sub-dimensions that mature in a stepwise fashion throughout one's life (Cloninger & Svrakic, 1997): Self-Directedness (SD; the ability for self-determination/will-power), Cooperativeness (CO; the capacity for

empathy/compassion for others) and Self-Transcendence (ST; individual differences in transpersonal experience and spirituality).

Cloninger has also described three sets of complex interactions among these traits, which can be summarized as a linked network of three cubes. The *temperament cube* involves interactions among NS, HA, and RD and the *character cube* involves interactions among SD, CO, and ST (Cloninger, 2004). These two cubes are linked via interactions of temperament (PS and HA) and character (SD) sub-dimensions and formulate the *resilience cube*. Within each cube, the different combinations of the sub-dimensions formulate multidimensional profiles (Table 1) that describe personality more accurately compared with their individual constituents (Cloninger et al., 2012).

Table 1

Description of the Temperament, Character, and Resilience profiles within each cube

	Profiles	Description
Temperament cube	Explosive (NHr)	Explosive: ambivalent, aloof, and quirky
	vs Reliable (nhR)	Reliable: stable, sociable, and traditional
	Adventurous (Nhr)	Adventurous: impulsive, oppositional, and quirky
	vs Cautious (nHR)	Cautious: inhibited, avoidant and traditional
	Sensitive (NHR)	Sensitive: ambivalent, avoidant, and attention-seeker
	vs Independent (nhr)	Independent: stable, oppositional, and private
	Methodical (nHr)	Methodical: inhibited, aloof and private
	vs Passionate (NhR)	Passionate: impulsive, sociable, and attention-seeker
Character cube	Schizotypal/Disorganized (scT)	Schizotypal/Disorganized: victimized, illogical and suspicious
	vs Organized (SCt)	Organized: leader, logical and conventional
	Apathetic (sct)	Apathetic: victimized, injudicious, and distrustful
	vs Creative (SCT)	Creative: leader, judicious and trustful
	Moody (sCT)	Moody: submissive, illogical, and trustful
	vs Bossy (Sct)	Bossy: dominant, logical, and distrustful
	Fanatical (ScT)	Fanatical: dominant, judicious, and suspicious
	vs Dependent (sCt)	Dependent: submissive, injudicious, and conventional
Resilience cube	Fragile (Hps)	Fragile: fatigable, half-hearted, and vulnerable
	vs Resilient (hPS)	Resilient: vigorous, industrious, and versatile
	High-strung (HpS)	High-strung: fatigable, free-wheeling, and deliberate
	vs Happy-go-lucky (hPs)	Happy-go-lucky: vigorous, ambitious, and carefree
	Laid-back (hps)	Laid-back: flexible, half-hearted, and carefree
	vs Conscientious (HPS)	Conscientious: inflexible, industrious, and deliberate
	Perfectionist (HPs)	Perfectionist: inflexible, ambitious, and vulnerable
	vs Self-reliant (hpS)	Self-reliant: flexible, free-wheeling, and versatile

**Note.* Capital letters in the personality profiles indicate high scores and lower-case letters indicate low scores in these traits (e.g., NHr, high Novelty Seeking, high Harm Avoidance, low Reward Dependence). C: Cooperativeness; H: Harm Avoidance; N: Novelty Seeking; P: Persistence; R: Reward Dependence; S: Self-Directedness; T: Self-Transcendence

Schizophrenia patients have been consistently described to present with increased HA and ST along with reduced NS, RD, PS, SD, and CO compared with control individuals (e.g., Fresán et al., 2015; Galindo et al., 2016; Hori et al., 2014; Jetha et al., 2013; Lee et al., 2016; Margetić et al., 2011; Miettunen et al., 2011; Miralles et al., 2014; Ohi et al., 2012; Sim et al., 2012; Smith et al., 2016; Song et al., 2013) and their unaffected relatives show an identical Temperament and Character profile (Galindo et al., 2016; Lee et al., 2016; Margetić et al., 2011; Sim et al., 2012; Smith et al., 2016). Although there are just a couple of studies, the "riskier" of the aforementioned

multidimensional profiles have been reported to be more prevalent in schizophrenia patients and their unaffected relatives (Molina et al., 2017) and to be associated with the development of increased paranoid ideation throughout life (Saarinen et al., 2018).

The individual temperament and character traits have also been associated with cognitive processes. For example, in non-clinical samples, several memory and IQ indices have been negatively associated with HA and positively with SD and CO (Hori et al., 2012), cognitive flexibility has been positively associated with PS (Hori et al., 2012) and HA but negatively associated with RD (Guillem et al., 2008). In schizophrenia patients, working memory and problem solving have been positively associated with SD while problem-solving has also been negatively associated with ST (Boeker et al., 2006). Working memory and crystallized IQ have been positively associated with SD and CO in nonpsychotic siblings of schizophrenia patients (Smith et al., 2008). As regards the associations of the multidimensional profiles with cognition, there is only one study in the general population indicating that the Explosive, Schizotypal, and Fragile profiles were associated with increased subjectively-reported cognitive lapses compared to their contrast groups (Giakoumaki et al., 2016). As cognitive processes are strongly associated with Prepulse Inhibition (PPI) of the startle reflex (e.g. Bitsios & Giakoumaki, 2005; Bitsios et al., 2006; Giakoumaki et al., 2006), a measure of sensorimotor gating (Braff et al., 1995), it is also of note that high ST and PS have been associated with reduced sensorimotor gating in healthy individuals (Takahashi et al., 2012) while so far there are no studies involving the effects of the multidimensional profiles.

Given the lack of studies on the multidimensional personality profiles, the aim of this study was to examine differences of the profiles in a wide range of cognitive functions and PPI in unaffected relatives of schizophrenia-spectrum patients and control individuals.

Methods

Participants

One hundred and thirty-nine unaffected first-degree relatives of patients diagnosed with a schizophrenia-spectrum disorder were recruited via the local psychiatric services and via advertisements in local media. We included offspring, siblings, and parents (the latter were included only if they had at least one sibling diagnosed with a schizophrenia-spectrum disorder) and they were all assessed with the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998). Exclusion criteria were (i) personal history of head trauma, medical or neurological conditions, (ii) current use of prescribed or recreational drugs, and (iii) personal history of DSM-IV Axis I disorders. Based on these criteria, nineteen relatives were excluded and one did not return the completed scale; therefore, the final sample consisted of 114 unaffected first-degree relatives (offspring: n=43, siblings: n=57, parents: n=14). One-hundred and twenty-two community participants (matched for gender, age, years of education, smoking habits, and Raven's raw score with the relatives) were also included in the study. This group also underwent psychiatric evaluation using the MINI and had identical exclusion criteria with the relatives, with the additional exclusion criterion of family (up to second-degree) history of DSM-IV Axis I disorders. A detailed description of the demographic characteristics of the two groups is presented in Table 2. One-hundred and eighty-seven participants (86 relatives and 101 controls) of the total sample were startle-responders (i.e. they had measurable startle responses); of the remaining participants, 35 were startle non-responders (16 relatives and 19 controls), 3 participants refused to undergo startle assessment and we could not estimate startle status in 11 participants due to equipment failure on the day of testing. Participants were tested in testing rooms at the University of Crete and each assessment lasted approximately 2.0 hours.

The present study was part of the Prefrontally-Mediated Endophenotypes in the Schizophrenia Spectrum (PreMES) study. The study was approved by the Research Ethics Committee of the University of Crete and the

Bureau for the Protection of Personal Data of the Greek State. After the presentation of the aims and procedures of the study and prior to participation, all participants gave written informed consent.

Assessment of Temperament and Character

Temperament and Character were assessed with the Greek version (Giakoumaki et al., 2016) of the Revised Temperament and Character Inventory (TCI-R; Cloninger, 1999). TCI-R is a 240-item self-report scale and items are rated in a five-point Likert scale, with responses ranging from “Definitely false” to “Definitely true”. Inaccurate/hasty responding is measured with five validation items; these do not ask whether respondents agree/disagree with a statement but require that they give a pre-specified response (e.g. "Please circle number four, this is a validity item") and are used to confirm that the respondents understand what they have to do and continue to pay attention to the task at hand. The items of the scale are organized into 29 sub-scales and the scores for the higher-order dimensions are the sum of the respective sub-scales.

Assessment of cognition

Cambridge neuropsychological test automated battery tasks (CANTAB; Robbins et al., 1998). CANTAB is a set of neuropsychological test batteries standardised in a large group of normal participants. The tests administered in this study were the Stockings of Cambridge (SoC), Stop Signal Task (SST), Spatial Working Memory (SWM), and Attention Switch Task (AST).

SoC is a modified, computerized version of the Tower of London task (Owen et al., 1990). Participants are required to compare two different arrangements of “balls” in “socks” (one presented on the top half of the screen, the other at the bottom half) and re-arrange (with the minimum possible number of moves), the balls in the lower half in order to match the target arrangement in the upper half. The problems are of increasing difficulty, starting with easy 2- and 3-move problems and proceeding with more difficult 4- and 5-move problems. Participants are required to plan the complete sequence of moves needed prior to their first move. Outcome variables were the number of problems solved correctly with the minimum moves, the mean number of moves, mean Initial thinking time (ITT; i.e. the time taken to plan the solution of the problem prior to the execution of the first move), and mean subsequent thinking time (STT; i.e. the time required for the execution of all subsequent moves).

In SST, a white ring is displayed on the screen to alert the participant and after a 500ms-delay period, an arrow is placed within the ring, pointing either to the left or to the right. Participants are required to press the right or left button of a pad according to the direction of the arrow. They are also instructed that whenever they hear a signal (a beeping noise), they should withhold their response and not press the buttons. The test includes 5 blocks and each one of them is divided into 4 sub-blocks, containing 12 go-trials (with no auditory stop-signal; go trials) and 4 stop-trials. Outcome variables were the total correct responses during the stop and go trials separately and the mean reaction time on go trials for the correct responses.

In SWM (Owen et al., 1990) participants are required to search through an increasing number of boxes randomly arranged on the screen, until they find a token that, at any one time, is hidden in one of the boxes. The key instruction is that once a token has been found within a particular box, that box should never be used again to hide a token. On each trial, every box is used once to hide a token such that the total number of tokens to be found corresponds to the number of boxes on the screen. Outcome variables were the number of between errors (i.e. times of re-visiting a box in which a token was previously found), within errors (i.e. times of re-visiting a box already found to be empty during the same search), double errors (i.e. errors categorized as both between and within) and strategy score (an efficient strategy is to follow a predetermined search sequence, beginning

with a specified box and then return to start each new sequence with that same box as soon as a token has been found; a high score indicates poor strategy).

AST assesses cued attentional switching. On every trial, an arrow appears on the left or the right half of the screen. A cue presented on the screen indicates whether the participant should make a response about the direction of the arrow or the side of the screen that the arrow was presented. Some trials display congruent stimuli (i.e. the arrow is on the right half of the screen and points to the right) whereas other trials display incongruent stimuli (i.e. the arrow is on the right half of the screen and points to the left), which require a higher cognitive demand. Outcome variables were congruency cost in mean correct responses (i.e. the difference between response latency of congruent versus incongruent trials; positive scores indicate that the examinee is faster on congruent trials while negative scores indicate that the examinee is faster on incongruent trials), switch cost in mean correct responses (i.e. the difference between response latency of non-switched versus switched trials; higher scores indicate that the examinee is faster on non-switched trials while lower scores indicate that the examinee is faster on switched trials), total correct responses in switched and non-switched trials respectively, total commission errors (i.e. the total number of trials in which the examinee responded either before the end of the window or before the appearance of the stimulus) is switched and non-switched trials respectively.

Stroop colour-word test (Golden, 1978). Participants are asked to read as quickly as possible in three 45sec consecutive periods, the names of colours written in black ink (Word score), then to name the colour of patterns (Colour score), and finally, to identify the colour of ink that is mismatched to a word (e.g. the word red printed in blue ink should be identified as blue; Colour-Word score). Outcome variables were the number of correct responses for each condition separately.

Wisconsin card sorting test (WCST; Nelson, 1976). A computerized version of the task was administered. The task consists of four stimulus cards that vary along three dimensions (colour, shape, and number) and a target card. Participants are asked to match the target card with one of the stimulus cards and feedback is provided after each match. The first match is always scored as correct and the rule used by the participant becomes the initial sorting principle. Once six consecutive cards are categorized correctly, the sorting principle changes, and are were informed of the shift in the sorting rule. The next match according to either of the two remaining sorting rules was also scored as correct and as previously, after six consecutive correct responses, the sorting principle again changes, and participants are informed of the shift in the sorting rule. The third match is scored as correct only when the last rule was used. After this, the participant is required to repeat the three rules in the same order. The task is discontinued when six categories are completed or when the target cards are exhausted. Outcome variables were the total number of completed categories, Milner-type and Nelson-type perseverative errors [Milner- type perseverative errors were defined as those that were correct on the immediately preceding stage of the test (Milner, 1963) and Nelson-type were all other perseverative errors (Nelson, 1976)], Milner- and Nelson-non perseverative errors, the total number of unrelated cards and the total errors.

Letter-number sequencing (LNS; Stogiannidou, 2014; Wechsler, 2008). Strings of intermingled letters and numbers are read to the participants and they are required to store and recite these strings after re-ordering the information (i.e. recite in numeric and alphabetical order). The strings are of increasing difficulty, starting with two digits/string and finishing with 8 digits/string. The outcome variable was the total number of correct strings.

Trail-making test (TMT; Zalonis et al., 2008). The task consists of two parts: in Part A, participants are required to connect consecutively numbered circles from 1 to 25 as quickly as possible; in Part B they are required

to connect 25 consecutively numbered and lettered circles by alternating between the two. Outcome variables were the time (in seconds) required to complete each part of the test.

Iowa gambling task (IGT; Bechara et al., 1994). Participants are instructed to select one card at a time from four decks (A, B, C, and D) displayed on a computer screen in order to win "pretend" money. Unknown to the participants, decks A and B are associated with high monetary rewards but also with high monetary losses while decks C and D have lower rewards but also lower penalties. The win or loss associated with the selection of a card appears on the screen. The outcome variables were the total number of cards selected from the advantageous decks C and D and the total number of cards selected from "risky" decks A and B.

Assessment of Prepulse Inhibition

The equipment, rejection criteria, and averaging procedures of the recordings as well as the calculation of %PPI are described in detail elsewhere (e.g. Giakoumaki et al., 2007, 2013). Pulses consisted of 40-ms, 115-dB white noise bursts, and prepulses consisted of 20-ms of either 75- or 85-dB white noise bursts over a 70-dB background noise. Three lead intervals were used (30, 60, and 120 ms). For each interval, there were six trials with the 75-dB prepulse and six with 85-dB prepulse at each lead interval. We chose to include two types of prepulses and three lead-intervals in our testing session due to the different processes tapped by different stimuli (Blumenthal, 1999; Putnam & Vanman, 1999). Recording began with 3 min of acclimation when only background noise was present. The recording period consisted of 48 trials: 12 Pulse-alone (PA) stimuli, 18 stimuli with the 75-dB prepulse (3 trials at each lead interval), and 18 stimuli with the 85-dB prepulse (3 trials at each lead interval). All trials were presented in a pseudorandom order with the constraint that no two identical trials occurred in succession. The inter-trial interval varied between 9 and 23 sec (average 15 sec).

Statistical analyses

Group differences between controls and relatives in demographic variables, TCI-R scores, and measures of the neuropsychological tasks were examined with either parametric or non-parametric analyses, according to the normality of the distribution; gender differences were examined with Pearson's chi-square. We formulated the multidimensional personality profiles by dividing our sample into participants scoring above or below the median for each Temperament/Character dimension. For these profiles, group differences in the measures of the cognitive tasks were examined with univariate analyses of variance or covariance, and group differences in %PPI were examined with repeated-measures analysis of variance (between-subjects factors: group and profile). To correct for multiple testing and reduce the probability of type I error, p values were Bonferroni corrected [0.05/10 (PPI and 9 cognitive tasks) = 0.005]. Therefore, we considered only p values ≤0.005, as significant and p values <0.01 as trends for significance.

Results

Demographics and TCI-R measures

In the total sample, there were no significant between-group differences in any demographic variable (all p values >0.09; for a detailed description see Table 2). In the sub-sample of startle responders, the controls were younger and had higher %PPI compared with the relatives (both p values <0.05). The group of relatives had higher HA [$F(1,235)=7.28$, $p<0.01$, Cohen's d=0.347] and ST [$F(1,235)=18.37$, $p<0.001$, Cohen's d=0.559] along with lower RD [$F(1,235)=7.59$, $p<0.01$, Cohen's d=0.358], PS [$F(1,235)=12.60$, $p<0.001$, Cohen's d=0.459], SD [$F(1,235)=7.71$, $p<0.01$, Cohen's d=0.360] and CO [$F(1,235)=8.63$, $p<0.005$, Cohen's d=0.381] scores.

Table 2
Demographic characteristics (mean±SD) of the control and unaffected relatives groups

	Controls (n=122)	Unaffected relatives (n=114)	P value
Age (years)[a]	33.10±10.16	35.54±12.02	>0.09
Education (years)[a]	14.94±2.15	14.36±3.52	>0.120
Cigarettes smoked daily[a]	5.72±8.91	5.22±9.85	>0.680
Gender (males:females)[b]	58:64	65:49	>0.140
Raven raw score[c]	50.16±7.81	48.91±9.80	>0.640

*Note [a]one-way ANOVA; [b]Pearson's chi-square comparison; [c]non-parametric Mann-Whitney comparison

Neuropsychological task performance between unaffected relatives and controls

When comparing the neuropsychological task performance of the two groups we found that the unaffected relatives (a) solved fewer problems (U= 4661.0, p<0.001) made more moves (U= 4275.5, p<0.001) and had prolonged mean STT (U= 4489.0, p<0.001) in SoC, (b) had higher mean reaction time in the "go trials" (U= 4729.0, p<0.001) of the SST, (c) made more within (U= 4827.5, p<0.001) and double (U= 5537.0, p<0.005) errors in SWM while there was also a trend for significantly poorer strategy (U= 5551.0, p<0.01) and between errors (U= 5536.5, p<0.001) in the same task (d) had fewer correct responses in the non-switched trials (U= 5178.5, p<0.005) of AST, (e) made more Milner non-perseverative errors (U= 5218.5, p<0.005) in the WCST, (f) gave fewer correct responses in LNS(U= 3948.0, p<0.001) and (g) had prolonged completion times in both parts of TMT (TMT A': U= 2174.5, p<0.001; TMT B': U= 2168.0, p<0.001). For a detailed description of both groups' performance in the neuropsychological tasks, see Table 3.

Personality profile analyses

In these analyses, we first checked for differences in demographics; when there were significant between-group differences in any variable, these were included as covariates in the examination of between-group differences.

Temperament Profiles

Explosive (NHr, n=25) vs ***Reliable*** (nhR, n=18). Univariate ANCOVAs with age as covariate (controls > relatives; p<0.05) revealed that the unaffected relatives solved fewer problems and made more moves in SoC, they had poorer performance in both parts of TMT and made more within errors in SWM (all p values <0.005). In the group of startle responders, repeated measures ANCOVA with age (controls > relatives; p<0.05) as covariate did not reveal any significant between-group differences or interactions involving either group or profile in PPI (all p values >0.120).

Adventurous (Nhr, n=26) vs ***Cautious*** (nHR, n=23). Univariate ANCOVAs with age as covariate (controls > relatives; p<0.005) revealed that the unaffected relatives made more Nelson type perseverative errors in the WCST and had poorer performance in both parts of TMT (all p values <0.005). In the group of startle responders (Adventurous n=23, Cautious n=18), repeated measures ANCOVA with age (controls < relatives; p <0.05) as covariate revealed higher PPI in the adventurous compared with the cautious profile [F(1,36)= 9.38, p= 0.004, η2= 0.207; Figure 1, upper left panel].

Table 3

Neuropsychological task performance (mean±SD) of the control and relatives groups

	Control group n= 122	**Relatives n=114**	**P value**
Stockings of Cambridge			
Problems solved[a]	9.55±1.81	8.42±1.98	**<0.001**
Mean moves[a]	4.00±0.44	4.34±0.55	**<0.001**
Mean ITT[a]	6007.43±3021.33	7185.70±4503.19	=0.033
Mean STT[a]	523.23±550.43	941.72±789.83	**<0.001**
Stop-Signal task			
Correct responses "go trials"[a]	238.50±1.90	236.89±18.00	=0.032
Mean RT "go trials"[a]	495.97±132.99	601.68±207.06	**<0.001**
Spatial Working Memory			
Between errors[a]	20.51±16.46	27.43±19.32	=0.007
Within errors[a]	2.10±3.86	5.72±10.20	**<0.001**
Double errors[a]	1.44±4.05	2.39±3.93	**=0.004**
Strategy[a]	38.44±5.83	40.80±7.74	=0.007
Attention Switch task			
Congruency cost[b]	103.04±69.86	107.02±81.75	0.689
Switch cost[b]	-74.71±105.26	-101.15±100.94	=0.052
Correct responses in switched trials[a]	76.70±6.99	77.23±7.30	=0.464
Correct responses in non-switched trials[a]	72.06±5.44	69.84±6.00	**=0.002**
Commission errors in switched trials[a]	0.11±0.41	0.15±0.53	=0.514
Commission errors in non-switched trials[a]	0.11±0.31	0.11±0.34	=0.871
Stroop Colour-word test			
Word score[b]	103.10±12.47	98.78±14.11	=0.013
Colour score[b]	72.89±10.02	70.05±12.21	=0.052
Colour-Word score[b]	45.06±8.54	42.43±10.43	=0.035
Wisconsin Card Sorting test			
Completed categories[a]	5.42±0.97	4.87±1.59	=0.019
Milner perseverative errors[a]	3.51±4.38	4.33±4.96	=0.290
Nelson perseverative errors[a]	2.10±2.17	3.30±4.05	=0.072
Milner non-perseverative errors[a]	3.42±3.68	4.89±4.36	**=0.002**
Nelson non-perseverative errors[a]	4.74±4.44	5.94±4.75	=0.025
Unrelated cards[a]	0.76±1.27	1.69±3.50	=0.631
Total errors[a]	8.74±9.11	10.91±9.18	=0.035
Letter-number Sequencing			
Correct responses[a]	11.40±2.80	8.96±3.19	**<0.001**
Trail-Making test			
Part A[a]	21.60±6.52	38.41±22.96	**<0.001**
Part B[a]	42.32±16.34	83.98±53.58	**<0.001**
Iowa Gambling task			
Cards A+B[a]	45.26±11.71	48.01±11.98	=0.057
Cards C+D[a]	54.65±11.80	52.01±11.96	=0.070

*Note. Significant differences between the profiles are marked in bold. ITT: Initial Thinking Time; RT: Reaction Time; STT: Subsequent Thinking Time [a]Non-parametric Mann-Whitney comparison; [b]One-way ANOVA

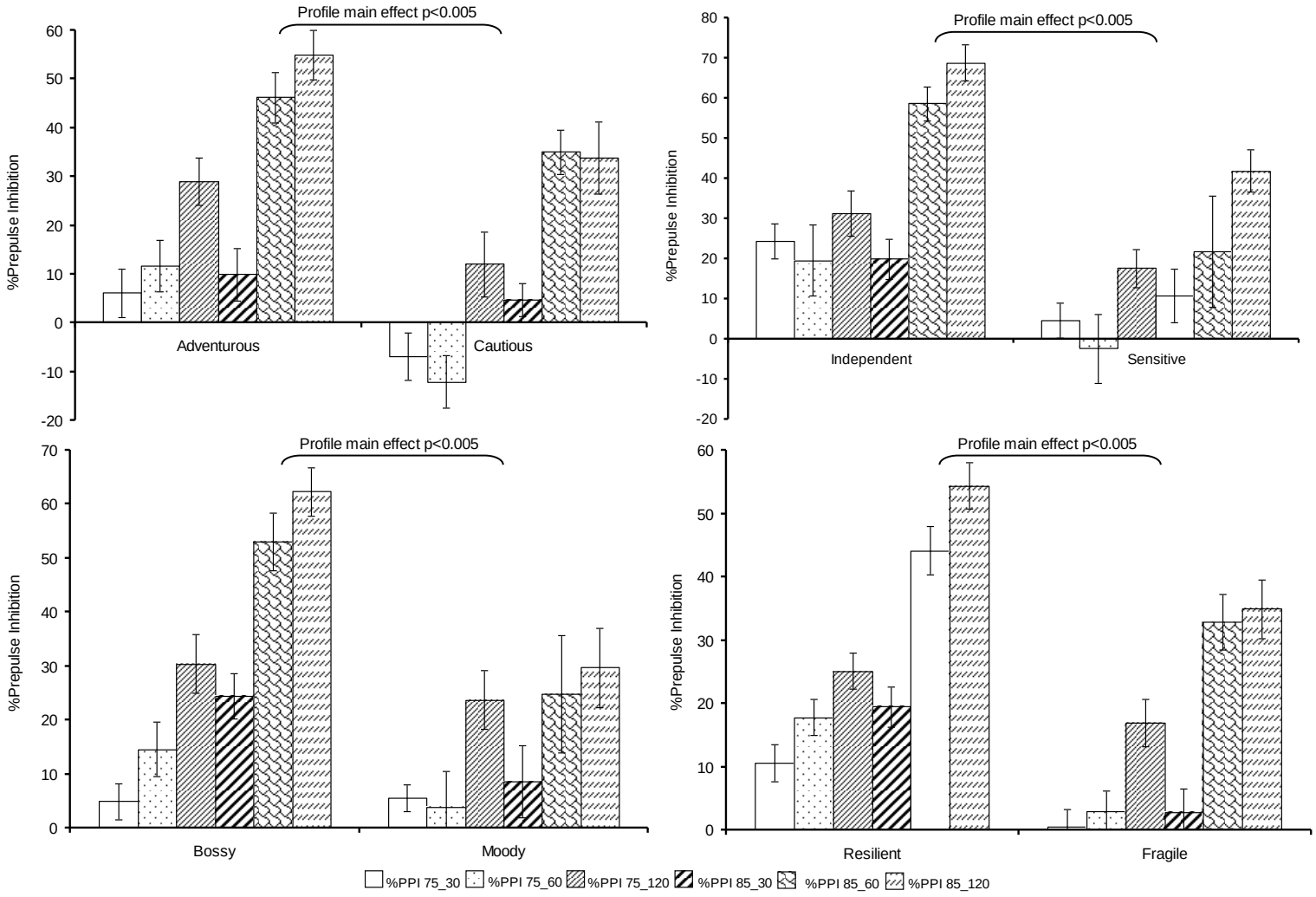

Figure 1. *Percentage Prepulse Inhibition in the Adventurous vs Cautious, Bossy vs Moody, Independent vs Sensitive and Resilient vs Fragile personality profiles*

Sensitive (NHR, n=16) vs ***Independent*** (nhr, n=20). Univariate ANOVAs showed that the unaffected relatives had worse strategy formation along with poorer performance in both parts of TMT and LNS (all p values <0.005). In the group of startle responders (Sensitive n=11, Independent n=13), repeated measures ANOVA revealed that the Sensitive profile had lower PPI compared with the Independent profile [F(1,20)= 13.05, p= 0.002, η2= 0.395; Figure 1, upper right panel].

Methodical (nHr, n=39) vs ***Passionate*** (NhR, n=42). The control group comprised more Passionate (n=24) and fewer Methodical (n=13) individuals compared with the relatives group (Passionate n=18, Methodical n=26; p<0.05). Univariate ANCOVAs with age as covariate (controls < relatives and Methodical > Passionate; both p values<0.05) revealed that the unaffected relatives had poorer performance in both parts of TMT and LNS (all p values <0.001) and selected more unrelated cards in the WCST (p=0.005). Significant Group x Profile interactions were revealed for the SoC total problems solved and mean moves (both p values <0.005) with the Passionate controls solving more problems and making fewer moves than the Methodical controls, while the opposite pattern was revealed for the unaffected relatives (i.e. Methodical relatives solved more problems and made fewer moves than Passionate relatives). In the group of startle responders, we did not find any significant between-group differences or interactions involving either group or profile in PPI (all p values >0.08).

Character Profiles

Schizotypal/Disorganized *(scT, n=47) vs* ***Organized*** *(SCt, n=42).* The control group comprised more Organized and fewer Schizotypal/Disorganized individuals compared with the relatives (p<0.001). Univariate ANOVAs revealed that the unaffected relatives made more within errors in SWM (p<0.005), had poorer performance in both parts of TMT (*both p* values <0.001), and tended to have lower LNS total correct responses (p<0.01). As regards the main effects of the profile, the Schizotypal/Disorganised individuals selected more cards from the risky decks of the IGT and fewer cards from the advantageous decks (both *p* values <0.005) compared with the Organised participants. In the group of startle responders, we found that the control group tended to have higher PPI [$F(1,64)= 7.03$, $p< 0.01$, $\eta^2= 0.099$] compared with the relatives.

Apathetic *(sct, n=28) vs* ***Creative*** *(SCT, n=33).* Univariate ANOVAs revealed that the unaffected relatives made more moves and had prolonged STT in SoC (both *p* values <0.005) along with poorer performance in both parts of TMT (both *p* values <0.001). They also tended to solved fewer problems in SoC and to produce fewer correct response in the LNS (both *p* values <0.01). As regards the main effects of the profile, the apathetic individuals made more commission errors in AST (p<0.005). Significant group x profile interactions were also found for (i) total problems solved and mean moves of SoC (both *p* values <0.005) with the Creative controls solving more problems and making fewer moves than the Apathetic controls while the opposite pattern was revealed for the relatives (i.e. Apathetic relatives solved more problems and made fewer moves than the Creative relatives), (ii) strategy score of SWM (p<0.005) with the Creative-controls having better performance than the Apathetic controls while, as previously, the opposite pattern was revealed for the unaffected relatives and (ii) total correct responses on switched trials of AST (p<0.005) with the Creative controls scoring higher than the Apathetic controls and again the opposite pattern was revealed for the group of relatives. In the group of startle responders, we did not find any significant between-group differences or interactions involving either group or profile in PPI (all *p* values >0.03).

Moody *(sCT, n=21) vs* ***Bossy*** *(Sct, n=26).* Univariate ANOVAs revealed that the unaffected relatives made more between errors (p<0.005) in SWM and had poorer performance in both parts of TMT and in LNS (all *p* values <0.001). In the group of startle-responders (Moody n=15, Bossy n=22), repeated measures ANOVA revealed that the Moody profile had lower PPI [$F(1,33)= 10.172$, $p= 0.003$, $\eta^2= 0.236$; Figure 1, (lower left panel) compared with the Bossy profile.

Fanatical *(ScT, n=8) vs* ***Dependent*** *(sCt, n=12)*. We did not proceed with the analyses due to the small sample sizes of the individual groups**.**

Resilience Profiles

Resilient *(hPS, n=55) vs* ***Fragile*** *(Hps, n=56)*. The control group comprised more Resilient than Fragile individuals compared with the relatives group ($p<0.05$). Univariate ANOVAs revealed that the unaffected relatives solved fewer problems, made more mean moves, and had prolonged STT in SoC along with poorer performance in both parts of TMT and LNS (all p values <0.001). The main effects of profile revealed that Fragile individuals made more commission errors in the AST ($p<0.005$) compared with the Resilient individuals. A significant Group x Profile interaction ($p<0.005$) indicated that the Resilient controls solved more problems in the SoC than the Fragile controls but the opposite pattern was revealed for the relatives (i.e. Fragile relatives solved more problems than the Resilient ones). In the group of startle responders (Fragile $n=46$, Resilient $n=46$), repeated measures ANCOVA with age as covariate (Fragile > Resilient; $p<0.05$) revealed that the Resilient profile had higher PPI [$F(1,87)= 0.23$, $p= 0.003$, $\eta^2= 0.096$; Figure 1, lower right panel] compared with the Fragile profile.

High-strung *(HpS, n=8) vs* ***Happy-go-lucky*** *(hPs, n=12)* and *Laid-back (hps, n=17) vs Conscientious (HPS, n=16)*. We did not proceed with the analyses due to the small sample sizes of the individual groups.

Perfectionist *(HPs, n=28) vs* ***Self-reliant*** *(hpS, n=28)*. Univariate ANCOVAs with age as covariate (controls < relatives; $p<0.05$) revealed that the unaffected relatives had prolonged mean STT in SoC, fewer correct responses in LNS, and prolonged completion times in both parts of TMT (all p values <0.005). In the group of startle-responders (Perfectionist $n=19$, Self-reliant $n=23$), repeated measures ANCOVA with age as covariate (controls < relatives; $p<0.05$) revealed that the control group tended to have higher PPI compared with the relatives [$F(1,37)= 5.48$, $p<0.05$, $\eta^2=0.129$].

Discussion

In support of the existing literature, we found that individuals at genetic risk for schizophrenia-spectrum disorders (i.e. unaffected first-degree relatives of patients) had a) higher HA and ST along with lower PS, SD, and CO scores (Galindo et al., 2016; Lee et al., 2016; Margetić et al., 2011; Sim et al., 2012; Smith et al., 2008), b) lower PPI (for a review see Thaker, 2008) and c) poorer cognition (for a review see Blokland et al., 2017) compared with individuals with no family-history of schizophrenia-spectrum disorders. We also report for the first time lower RD in the group of unaffected relatives. We did not find a group difference in NS, which is in accordance with previous studies (Galindo et al., 2016; Sim et al., 2012, Smith et al., 2008) and the low heritability and familial aggregation rates of this Temperament dimension in schizophrenia (Lee et al., 2016).

When examining the multidimensional Temperament and Character profiles, we found an unequal distribution of relatives and controls in several “disadvantageous” profiles: the Methodical (i.e. individuals who are hesitant, distant and introverted), Schizotypal/Disorganized (i.e. referring to victimized, irrational and suspicious people), Fanatical (i.e. describing authoritative, judicious and suspicious individuals) and Fragile (i.e. individuals who are fatigable, half-hearted and vulnerable) profiles comprised more relatives than controls compared with their counterparts (Passionate, Organized, Dependent and Resilient, respectively). Overall, all of these profiles are easily associated with the schizophrenia-spectrum as they either describe or have been associated with the presence of attenuated symptoms of the spectrum. Thus, the characteristics of the Methodical profile describe attenuated negative symptoms, the characteristics of the Schizotypal/Disorganized profile closely

resemble positive symptoms, the Fanatical profile has been associated with paranoid traits (Cloninger et al., 1999) and the Fragile profile has been associated with high schizotypy (Giakoumaki et al., 2016).

When comparing the multidimensional profiles in cognitive processes, we found that the Organized profile had higher emotional decision making and the Creative profile made fewer commission errors in the attention switching task compared with their counterparts (Schizotypal/Disorganized and Apathetic, respectively); the "hybrid" Resilient profile also made fewer commission errors in the attention switching task compared with the Fragile profile. The "common link" between the Organized, Creative, and Resilient profiles is the prevalence of high SD. Although the literature is still sparse in the field, these findings are in accordance with previous reports of higher incidence of self-reported cognitive failures in Schizotypal and Fragile individuals (Giakoumaki et al., 2016) and negative associations between SD and emotional decision making (Forbush et al., 2008), attentional set-shifting (Bergvall et al., 2003) and several memory indices (Boeker et al., 2006; Hori et al., 2012; Rönnlund et al., 2011; Smith et al., 2008).

Counter-intuitive interactions between group membership and profile were revealed: a) Passionate controls had superior planning/problem-solving abilities compared with the Methodical controls, but the Methodical relatives scored higher compared with their counterpart; b) Creative controls had superior planning/problem-solving abilities along with superior strategy formation and attention switching compared with Apathetic controls, but the Apathetic relatives outperformed Creative relatives and c) Resilient controls had superior planning/problem-solving abilities than the Fragile controls, but the Fragile relatives outperformed the Resilient ones. The fear of developing the disorder experienced by relatives of schizophrenia patients is known to be high (Stålberg et al., 2004). Thus, although highly speculative, we propose that being either a Methodical or Apathetic or Fragile relative of schizophrenia patients might "work the opposite way" than being a Methodical or Apathetic or Fragile control as regards cognition: as the relatives get acquainted with schizophrenia (e.g. early signs, heritability rates, treatment outcomes, etc) their "risky" temperament and character characteristics might function as adaptive/coping mechanisms instead of maladaptive traits that help them overcome their daily difficulties and they eventually present with superior cognitive processes that involve the ability to efficiently find alternatives (i.e. planning/problem solving, strategy formation, attentional set-shifting).

Finally, for the first time we found that the Adventurous, Independent, Bossy, and Resilient profiles had higher PPI compared with their counterparts (i.e. Cautious, Sensitive, Moody, and Fragile profiles). This finding is in accordance with (a) evidence suggesting that the Cautious profile is indicative of dependent personality disorder (Svrakic et al., 2002), which has been associated with reduced PPI (Franklin et al., 2009) and (b) associations of the Moody profile with bipolar disorder (Cloninger et al., 1998), which is also characterized by impaired PPI [Giakoumaki et al., 2007; Sánchez-Morla et al., 2016).

To conclude, in the present study we found for the first time that certain "disadvantageous" multidimensional Temperament/Character profiles (a) are more prevalent in unaffected relatives of schizophrenia-spectrum patients compared with control individuals and (b) are characterized by poor planning/problem solving, strategy formation and attention switching irrespective of the genetic loading for schizophrenia-spectrum disorders. We also replicated previous findings on differences between unaffected relatives of schizophrenia spectrum patients and control individuals in Temperament/Character dimensions, cognitive processes, and PPI. These findings could have implications in intervention and psychoeducation programs in schizophrenia. The limitations of the study include its cross-sectional nature and mainly the small sample sizes per multidimensional personality profile. There is also some degree of heterogeneity in the group of relatives (we included parents, siblings, and offspring who do not carry the same degree of genetic-risk) and

we did not control for genetic factors implicated in both the schizophrenia-spectrum as well as in Temperament and Character.

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ΕΜΠΕΙΡΙΚΗ ΕΡΓΑΣΙΑ | RESEARCH PAPER

Οι σχέσεις των πολυδιάστατων προφίλ ιδιοσυγκρασίας και χαρακτήρα με τις γνωστικές λειτουργίες και τον αισθητικοκινητικό ηθμό σε ανθρώπους με κίνδυνο εκδήλωσης διαταραχών στο φάσμα της σχιζοφρένειας: Αρχικά ευρήματα

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γνωστικές λειτουργίες, ιδιοσυγκρασία και χαρακτήρας, πολυδιάστατα προφίλ, προπαλμική αναστολή, σχιζοφρένεια

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ΠΕΡΙΛΗΨΗ

Το βιοψυχολογικό μοντέλο του Cloninger για την προσωπικότητα κάνει διάκριση ανάμεσα σε γνωρίσματα Ιδιοσυγκρασίας [Αναζήτηση Νέων Εμπειριών, Αποφυγή Βλάβης, Εξάρτηση από την Ανταμοιβή, Επιμονή] και Χαρακτήρα [Αυτό-Κατευθυντικότητα, Συνεργασιμότητα, Αυτό-Υπέρβαση]. Ο Cloninger έχει περιγράψει τρεις ομάδες πολύπλοκων αλληλεπιδράσεων μεταξύ των γνωρισμάτων, που συνοψίζονται σε ένα δίκτυο τριών αλληλοσυνδεόμενων κύβων. Σε κάθε κύβο, οι διαφορετικοί συνδυασμοί των επιμέρους γνωρισμάτων της προσωπικότητας σχηματίζουν πολυδιάστατα προφίλ, που περιγράφουν την προσωπικότητα ακριβέστερα σε σχέση με τα μεμονωμένα γνωρίσματα. Ο στόχος της παρούσας μελέτης ήταν η διερεύνηση διαφορών ανάμεσα στα πολυδιάστατα προφίλ ως προς τις γνωστικές λειτουργίες και την Προπαλμική Αναστολή (ΠΠΑ) σε μη-νοσούντες συγγενείς ασθενών στο φάσμα της σχιζοφρένειας και στον υγιή πληθυσμό. Αξιολογήσαμε 114 συγγενείς και 122 συμμετέχοντες από τον γενικό πληθυσμό ως προς τα γνωρίσματα της προσωπικότητας, ένα εύρος γνωστικών λειτουργιών και την ΠΠΑ. Η ομάδα των συγγενών είχε υψηλότερη βαθμολογία στην Αποφυγή Βλάβης και την Αυτό-Υπέρβαση, χαμηλότερη βαθμολογία στην Εξάρτηση από την Ανταμοιβή, την Επιμονή, την Αυτό-Κατευθυντικότητα και την Συνεργασιμότητα, χαμηλότερη ΠΠΑ και φτωχότερη γνωστική λειτουργικότητα. Βρήκαμε, επίσης, α) διαφορές στην κατανομή των συγγενών και των συμμετεχόντων της ομάδας ελέγχου σε πολλά «επικίνδυνα» προφίλ, β) ότι τα προφίλ των Σχιζοτύπων/Αποδιοργανωμένων, των Αδιάφορων και των Ευαίσθητων συμμετεχόντων είχαν φτωχότερη ικανότητα για λήψη αποφάσεων με συναισθηματική ανάδραση και εναλλαγή της προσοχής, αντίστοιχα και γ) τα προφίλ των Περιπετειωδών, των Ανεξάρτητων, των Αυταρχικών και των Ανθεκτικών συμμετεχόντων είχαν χαμηλότερη ΠΠΑ. Τα ευρήματα αναδεικνύουν τον καθοριστικό ρόλο των παραγόντων της προσωπικότητας στις γνωστικές λειτουργίες και έχουν πιθανές εφαρμογές σε προγράμματα πρώιμης παρέμβασης στο φάσμα της σχιζοφρένειας.