Psychobiological personality traits of children and adolescents with disorders of arousal

Katherine Turner[a]* & Anna Castelnovo[b,c,d]*, Lampros Perogamvros[e,f], Robert C. Cloninger[g], Alessia Bertolotti[h], Andrea Galbiati[h], Paola Proserpio[i], Michele Terzaghi[l,m], Luigi Ferini Strambi[h], Raffaele Manni[m], Lino Nobili[n,o], Mauro Manconi[b,c,p], Maria Paola Canevini[a,q], Elena Zambrelli[a]

*These two authors contributed equally to the manuscript

[a]Epilepsy Center - Sleep Medicine Center, Childhood and Adolescence Neuropsychiatry Unit, ASST Santi Paolo e Carlo, San Paolo Hospital, Milan, Italy

[b]Sleep Medicine, Neurocenter of Southern Switzerland, Regional Hospital of Lugano, Lugano, Switzerland

[c]Faculty of Biomedical Sciences, Università della Svizzera Italiana, Lugano, Switzerland

[d]University Hospital of Psychiatry and Psychotherapy, University of Bern, Switzerland

[e]Center for Sleep Medicine, University Hospitals of Geneva, Geneva, Switzerland

[f]Department of Psychiatry, University Hospitals of Geneva, Geneva, Switzerland

[g]Department of Psychiatry, Washington University School of Medicine, St. Louis, Missouri, United States of America

[h]Sleep Disorders Center, Department of Neurology, Scientific Institute Ospedale San Raffaele, and "Vita-Salute" San Raffaele University, Milan, Italy

[i]Department of Neuroscience, Sleep Medicine Centre, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

[l]Unit of Sleep Medicine and Epilepsy, IRCCS Istituto Mondino Foundation, Pavia, Italy

[m]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy

[n]Child Neuropsychiatry, IRCCS G. Gaslini Institute, Genoa, Italy

[o]Department of Neuroscience – Rehabilitation–Ophthalmology – Genetics – Child and Maternal Health (DINOGMI), University of Genoa, Italy

[p]Department of Neurology, University Hospital, Inselspital, Bern, Switzerland

[q]Department of Health Sciences, University of Milan, Italy

Corresponding author: Kathrine Turner: Via Antonio di Rudinì 8, 20142, Milan, Italy. Email: katherine.turner@asst-santipaolocarlo.it

ABSTRACT

Disorders of arousal (DOA) are Non-Rem Sleep (NREM) parasomnias that emerge from incomplete arousal out of deep sleep and lead to a broad variety of emotional and motor behaviours. Increasing evidence supports the hypothesis that specific psychopathological traits contribute to the multifactorial origin of these phenomena. The aim of the current multicenter study was to compare the personality profile of children and adolescents with and without DOA using the Junior Temperament and Character Inventory (JTCI).

We enrolled 36 patients with a diagnosis of DOA (mean age of 11 ± 3 years, 64% males), and 36 healthy age and gender matched control subjects (mean age of 11.2 ± 3.6, years, 67% males). Their parents completed the Paris Arousal Disorder Severity Scale (PADSS), the Sleep Disturbance Scale for Children (SDSC) and the JTCI.

Patients with DOA reached significantly higher levels compared to their control group in total PADSS ($p < .0001$) and in total SDSC ($p < 0.0001$). They also displayed higher scores in novelty seeking ($p = 0.005$), harm avoidance ($p = 0.01$), self-transcendence ($p = 0.006$) JTCI subscales, and lower scores on the self- directedness subscale ($p = 0.004$).

Our pediatric sample with DOA exhibited specific psychobiological personality traits compared to age and gender matched subjects without DOA. These results shed light on new possible etiopathogenetic mechanisms, as TCI traits have been linked to specific genetic variants and brain circuits, like the reward system. Prospective studies are required to assess the effect of targeted psychological/psychiatric treatment on DOA symptomatology.

Keywords: NREM sleep parasomnias; psychopathology; sleepwalking; somnambulism; sleep terrors; confusional arousal

Word count:

Tables: 1

Figures: 1

Number of References: 50

1. Introduction

"Disorders of arousal" (DOA) are Non-Rem Sleep (NREM) parasomnias characterized by involuntary behaviours of variable complexity that occur during partial (local) awakenings from NREM sleep (American Academy of Sleep Medicine, 2014). Pathological behaviours include sitting up in bed quietly, looking around or staring at the dark with a fixed gaze or with an expression of fear /surprise, crying, speaking or wandering or running out of a door or window (Zadra *et al.*, 2013). These nocturnal episodes typically have onset during childhood with a prevalence ranging from 13% to 39% (probably related to the abundance of slow-wave sleep at this age) and their prevalence tends to decrease with age (Laberge *et al.*, 2000), reaching 1-4% during adulthood (Stallman and Kohler, 2016).

Current diagnostic criteria are: 1) recurrent episodes of incomplete awakening from sleep, 2) inappropriate or absent responsiveness to efforts of others to intervene or redirect the person during the episode, 3) limited or no associated cognition or dream imagery and 4) partial or complete amnesia for the episode. According to the 3rd International Classification of Sleep Disorders (ICSD-3), American Academy of Sleep Medicine, 2014), this group of disorders includes 3 subtypes: confusional arousals (CA), sleep terrors (ST) and sleepwalking (SW). However, these entities share a similar familiar/genetic background and may vary along a continuum in the same patients across different episodes and at different ages.

Although traditionally considered benign, DOA may lead patients to inadvertently hurt themselves or others during their episodes (Ohayon and Schenck, 2010), are associated with a higher frequency of excessive daytime sleepiness (Lopez, Jaussent and Dauvilliers, 2014) and may cause distress and shame to affected patients (Arnulf *et al.*, 2014). The diagnosis and treatment of these disorders still suffers from the lack of a clear understanding of their underlying neurobiological mechanisms. The origin is thought to be multifactorial and to derive from the sum of predisposing – mainly genetic factors (Lecendreux *et al.*, 2003; Licis *et al.*, 2011; Heidbreder *et al.*, 2016), priming factors such as nocturnal sleep deprivation (Pilon, Montplaisir and Zadra, 2008), and precipitating factors, as external

or internal sensory stimuli (Guilleminault *et al.*, 2005) or even stressful life-events (Lecendreux et al., 2003).

Despite of the common complaint by patients of an association between DOA symptoms and their psychological state and/or stress (Szelenberger, Niemcewicz and Dabrowska, 2005; Castelnovo et al., 2021), the literature on this relationship is currently limited and controversial. When looking more specifically to children, the existing studies are even sparser than those existing for adults, although more consistent in terms of results, and overall suggest a link with psychopathology and especially with anxiety (Dollinger, 1982; Klanckenberg, 1982; Fisher and Wilson, 1987; Gau and Suen Soong, 1999; Laberge et al., 2000; Petit et al., 2007; Castelnovo et al., 2021). The working hypothesis is that specific psychobiological features may represent a priming factor, exacerbating the intensity and frequency of DOA clinical episodes in predisposed subjects, either directly (e.g., altered brain circuits and neuro modulation) or indirectly (causing fragmented sleep, for example) (Castelnovo et al., 2021). This hypothesis requires difficult longitudinal perspective and experimental studies. Nonetheless, as a first step, an association between psychological/psychiatric factors should be more firmly established.

The general aim of the current study was to compare the personality profile of children and adolescents with and without DOA using the Junior Temperament and Character Inventory. More specifically, on the basis of one previous study on TCI in parasomnias (DOA and nightmares) in adults (Perogamvros *et al.*, 2015), we expected higher scores on the Novelty Seeking (NS) TCI scale and lower scores on the Self-directedness (SD) TCI scales in patients with DOA compared to control participants. These personality traits have a known neurobiological foundation, have been associated with specific genetic variants and have been linked to reward-related brain functions.

2. Material and methods

This is a multicenter case control study that involved 5 Sleep Centers: the “Santi Paolo e Carlo” hospital (Milan, Italy), the “Grande Ospedale Metropolitano Niguarda” hospital (Milan, Italy), the

IRCCS San Raffaele Hospital (Milan, Italy), the IRCCS Mondino Foundation (Pavia, Italy), and the Civic Regional Hospital of Lugano (Lugano, Switzerland, Italian language), over a span of 2 years. This study was approved by the ethic committee of each Center (leaded by the coordinator center in the "Santi Paolo e Carlo" Hospital). All caregivers gave their informed written consent before being enrolled in the study. All study procedures were conducted in accordance with the Declaration of Helsinki.

2.1 Participants

Consecutive patients with a diagnosis of DOA (SW, ST and CA) were recruited and prospectively evaluated within this study. This population partially overlaps with the one presented in a previous study by our groups on Child Behavior Check-List (CBCL) in DOA (Castelnovo et al., 2021). A detailed history was taken by a physician expert in sleep medicine with patients and/or cohabitants (parents, caregivers). Inclusion criteria for the patient group included: 1) a typical history of DOA, according to ICSD-3 criteria (American Academy of Sleep Medicine, 2014); 2) at least one episode in the past year; 3) age between 6 to 18 years old; 4) fluency in the Italian language (patients/parents or caregivers). Exclusion criteria were: 1) a diagnosis of parasomnia due to a medical disorder or due to a medication or substance; 2) intellectual disability; 3) epilepsy and other major neurologic co-morbidities and 4) sleep breathing disorders as suspected from clinical history and verified by video-polysomnography (v-PSG).

Control healthy participants were recruited through advertisement in primary and secondary schools or by word of mouth among investigators' relatives, colleagues and friends. Healthy control subjects were matched for sex and age to DOA patients. None of them reported any current or past episodes of parasomnias, neither a familiar history of DOA, or other known sleep disorders or sleep complaints. We excluded patients with intellectual disability and major neurological disorders.

The parents of 36 patients and of 36 age and gender-matched control participants filled in a series of questionnaires in order to evaluate potential abnormal nocturnal behavioral episodes (Paris Arousal

Disorder Severity Scale "PADSS", Arnulf et al., 2014), sleep problems (Sleep Disturbance Scale for Children "SDSC", Bruni et al., 1996), as well as the personality profiles (Junior Temperament and Character Inventory, "JTCI") of their children (Cloninger et al., 1994; Andriola et al., 2012).

2.2 Questionnaires

Paris Arousal Disorder Severity Scale (PADSS)

The PADSS is a rater-administered questionnaire (filled by the patients' parents or whoever takes their place) validated to be used for screening DOA, as well as for monitoring DOA severity and treatment efficacy (Arnulf *et al.*, 2014). It consists of 24 items divided in three subscales: 1) PADSS-A, an inventory of the most problematic parasomnia behaviors listed in order of severity, 2) PADSS-B, which evaluates the frequency of the episodes (from never to 1 every night) and 3) PADSS-C to investigate the negative consequences of DOA, like being tired the next day, feeling ashamed or self or hetero-inflicted injuries. The pathological cut-off is 13/14 and has high sensitivity (83.6%) and specificity (87.8%) for DOA.

Sleep Disturbance Scale for Children (SDSC)

The SDSC Sleep Disturbance Scale for Children (Bruni *et al.*, 1996) is a self-administered questionnaire to assess sleep disturbances in children and adolescents. It consists of 26 items in a Likert-type scale with values from 1 to 5 (higher values reflect a higher frequency), which allows to extract 6 categories of sleep disorders. It screens for difficulties in initiating and maintaining sleep (DIMS), sleep-breathing disorders (SBD), disorders of arousal and nightmares (DA), sleep wake transition disorders (SWTD), disorders of excessive somnolence (DOES), sleep hyperhidrosis (SHY). The total score is the sum of the 26 items (range 26-130). A T-score $\leq$70 is considered normal. Cut-off scores are: $\geq$ 51 for the SDSC raw score, $\geq$16 for DIMS, $\geq$7 for SBD, $\geq$5 for DA, $\geq$14 for SWTD, $\geq$13 for DOES and $\geq$6 for SHY. In order to evaluate the prevalence of pathological items in the SDSC, the results were classified into pathological, borderline or normal, using a cut-off value according to the validation criteria of the test.

Junior Temperament and Character Inventory (JTCI)

The JTCI is a questionnaire containing 107 statements regarding tastes, interests, emotional reactions, attitudes, goals, and values. The response mode of this TCI version is binary and provides a choice between “true” or alternatively "false" (Cloninger et al., 1994). The Italian version of the JTCI was developed for the personality assessment in Italian subjects aged 6 to 16 according to the Cloninger's psychobiological model (Andriola *et al.*, 2012).

The questionnaire takes into consideration 7 major dimensions, divided into 2 domains: Temperament and Character. Temperament traits are evaluated through 4 dimensions (Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), Persistence (P), and character traits are: Self-Directedness (SD), Cooperativeness (CO) and Self-Transcendence (ST) (Cloninger et al., 2019; Zwir, Arnedo, et al., 2020b; Zwir, Mishra, et al., 2020).

Novelty seeking (NS) is a tendency to initiate appetitive approach in response to novel signals, even if they do not predict rewards (Zwir, Arnedo, *et al.*, 2020b). Novelty seekers are exploratory, impulsive, extravagant, and disorderly. Harm avoidance (HA) involves the inhibition of behaviour in response to signals of punishment or loss of reward. Harm avoidant individuals are pessimistic worriers, fearful, shy, and fatigable. Reward dependence (RD) is the tendency to have a marked response to signals of social reward. Reward dependent individuals are sentimental, sociable, seek social approval, and form warm attachments. Persistence (P) involves reward-seeking behaviour despite frustration. Persistent individuals are described as hardworking, ambitious, and determined to complete tasks despite frustration and fatigue. Self-directedness (SD) expresses the individual’s sense of resourcefulness, purpose, and responsibility, and those who are low in Self-directedness are often described as having weak self-control. Cooperativeness (CO) is characterized by being tolerant, helpful, empathic, and compassionate. Self-transcendent (ST) individuals are characterized by being idealistic, easily absorbed in the moment, contemplative, and spiritual. Self-transcendence involves a capacity to derive pleasure from valued actions by identifying with what is greater than one’s individual self.

2.3 Video-polysomnography

Selected patients (n = 24) underwent one-night video-polysomnography recording (v-PSG) in order to exclude other sleep problems. The vPSG montages included: extended EEG montages (full-scalp EEG, positioning of leads according to the International 10-20 System, 2 electrooculograms (EOG), one chin electromyogram (EMG), EMG of the right and left tibialis anterior muscles, an electrocardiogram (ECG), pulse-oximetry, snoring and video. All vPSG were visually scored on 30 s epochs following standard American Academy of Sleep Medicine Criteria by an expert in sleep medicine (Berry *et al.*, 2017).

Recorded subjects who had a comorbid sleep disorder were excluded from the current analysis.

None of the controls were recorded by v-PSG. Control subjects with a clinical doubt of any underlying sleep disorder from the clinical screening were discarded.

2.4 Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics 27.0. Quantitative data were expressed as mean and standard deviation (SD). Qualitative data were reported as absolute frequencies and percentages.

A T-test of Student was used to assess the differences between the mean values in the 2 groups (DOA and healthy controls). Normality of the data and homogeneity of variances were tested by the Shapiro-Wilk test and Levene's test, respectively.

The association between DOA severity and TCI scores was assessed using Spearman correlation.

Statistical significance was set at $p < 0.05$. Bonferroni’s correction was used to adjust for multi-comparison. Effect sizes were interpreted using Cohen’s benchmarks.

3. Results

Thirty-six patients with a diagnosis of DOA (mean age of 11.0 ± 3.0 years, range: 7-18 years; 23 [63.9%] of 36 males) and 36 healthy matched controls (mean age of 11.2 ± 3.6, years, range: 6-18 years; 24 [66.7%] of 36 males) were included in the study. Twenty-two (61.1%) had a diagnosis of SW, 4 (11.1%) of SW and ST, 4 (11.1%) of SW and CA, 2 (5.5%) of CA, 2 (5.5%) of ST, 1 (2.8%) of ST and CA and 1 (2.8%) a combination of these three DOA subtypes. The mean age of onset was 5 ± 2.2 years (range 1-10). A family history for sleep disorders was documented in 23 cases (63.9%). Six had associated bruxism, 6 sleep enuresis, 5 sleep talking, 1 insomnia, 2 of restless leg syndrome (RLS) and 1 had periodic limb movements without a diagnosis of RLS. Thirteen (36,1%) had other neuro-psychiatric comorbidities: 9 had an Attention Deficit Hyperactivity Disorder (ADHD), 1 of them had also oppositional defiant disorder, 1 a conduct disorder, 3 a Specific Learning Disorder (SLD). Four patients had SLD without other neuro-psychiatric comorbidities. Nine (25%) were under treatment: 4 were taking Melatonin, 2 Hydroxytryptophan, 2 Melatonin and Hydroxytryptophan. Moreover, one patient was under pharmacological treatment for comorbid ADHD with low dose Aripiprazole.

3.1 Questionnaires

PADSS

DOA patients had a significantly higher total PADSS scores (mean = 10.94 ± 5.61, $p < 0.0001$) compared to the control group (mean = 0.77 ± 1.82). Additionally, DOA patients obtained significantly higher scores for all sub-scales: PADSS-A ($p < 0.0001$), PADSS-B ($p < 0.0001$) and PADSS-C ($p < 0.0001$, Table 1).

SDSC

Mean SDSC total score was 76.0 ± 17.96 in DOA patient's group and 50.2 ± 7.79 in the control group ($p < 0.0001$). The 2 groups showed a statistically significant difference in all the factors scores ($p < 0.05$), and remained significant after Bonferroni's multiple comparison correction ($p < 0.007$), except for SBD. Results are summarized in Table 1.

JTCI

The DOA group displayed higher scores on JTCI subscales novelty seeking (DOA patients mean = 9.00 ± 3.44 vs. controls mean = 6.83 ± 2.98, p = 0.005), harm avoidance (DOA patients mean = 10.35 ± 5.17 vs. controls mean = 7.58 ± 4.34, p = 0.011), self-transcendence (DOA patients mean = 2.56 ± 1.32 vs. controls mean = 1.72 ± 1.37, p = 0.006) and lower scores on the self-directedness subscale (DOA patients mean = 12.84 ± 5.73 vs. controls mean = 16.06 ± 3.32, p = 0.004, Table 1, Figure 1). After Bonferroni's correction ($p<0.007$), harm-avoidance was no longer significant.

No differences were found on dimensions of reward dependence (DOA patients mean = 5.81 ± 1.87 vs controls mean = 5.86 ± 1.88, p = 0.9), persistence (DOA patients mean = 2.56 ± 1.68 vs. controls mean = 3.27 ± 1.64, p = 0.07), and cooperativeness (DOA patients mean = 15.2 ± 4.31 vs. controls mean = 15.69 ± 2.2, p = 0.6).

There were no significant correlations between the JTCI and DOA severity.

4. Discussion

In this study, we performed a detailed psychometric examination of children with DOA by using the JTCI, a modified version of the adult TCI, validated and adapted for children and adolescents.

We found that DOAs are associated with a specific personality profile, which could largely make these individuals more susceptible for these disorders due to the strong heritability of temperament traits (Cloninger *et al.*, 2019). More specifically, compared to control subjects, children with DOA were characterized by high Novelty Seeking, Harm Avoidance and Self-Transcendence, and low Self-Directedness. Before providing more details about the interpretation of these results, one should consider that the learning systems underlying TCI are best tapped by profiles (combination of dimensions) and not by the individual dimensions alone. A combination of high Novelty Seeking, Harm Avoidance and low Self-Directedness suggests elevated impulsivity, approach-avoidance conflicts, and emotional instability, as in cluster B personality disorders according to DSM-5 (Cloninger, 2002a). More specifically, the co-occurrence of high Novelty Seeking and Harm Avoidance indicates the presence of approach-avoidance conflicts, which at the presence of low Self-

Directedness and high Self-Transcendence, reflect a vulnerability to magical thinking and schizotypy (Smith *et al.*, 2008). The individuals with this profile are usually open to odd ideas and behaviours, associated with distorted perceptions of reality (Laidlaw *et al.*, 2005). These findings are thus in accordance with previous studies showing increased impulsivity (Bonkalo, 1974; Schmidt, Gay and van der Linden, 2008), emotionality (Hartmann E, 1989; Schredl *et al.*, 1999), dissociation (Giesbrecht and Merckelbach, 2004) and low mindfulness (Simor *et al.*, 2011) in parasomnias. Moreover, low Self-Directedness has also been associated with higher mood distress, anxiety and perceived stress (Laidlaw *et al.*, 2005), factors which are often encountered in sleepwalkers (Ohayon, Guilleminault and Priest, 1999; Laberge *et al.*, 2000; Castelnovo *et al.*, 2021). Interestingly, both abnormalities in the sensitivity to reward and to goal conflicts and an enhanced negative coping trait (ie, anxious rumination) associated with an increase in adjusted left PCC volume, were also recently reported in DOA adult patients (Ramm *et al.,* 2020).

A study (Perogamvros *et al.*, 2015) using TCI in adult patients with parasomnias (sleepwalkers and nightmares) found similar results regarding the specific personality profile of DOA patients. Compared to controls, adult parasomnia patients (12 sleepwalkers and 12 patients with idiopathic nightmares) scored higher on Novelty Seeking and in particular on the exploratory excitability/curiosity (NS1) subscale, and lower on Self-Directedness, suggesting a general increase in reward sensitivity and impulsivity, as in our group of children and adolescents. As the sample size of the current study is larger than the one in the adult population (that comprised only 12 patients with sleepwalking and 12 patients with nightmares), it allows for a solid confirmation of the previous characterization of psychopathological and personality traits of DOA patients. Furthermore, adult parasomnia patients tended to worry about social separation, as indicated by greater anticipatory worry (HA1) and dependence on social attachment (RD3). This indicates that adult sleepwalkers are likely to act impulsively to seek social attachment, and may be hypersensitive to the loss of social support. Moreover, we know that anxiety, stress or high levels of insecurity increase the occurrence of parasomnia episodes in both children and adults, supporting that sleepwalking/sleep terrors

constitute a partial hyperarousal reflecting an ancient *survival* mechanism at work (Perogamvros *et al.*, 2020). As the combination of high HA1 (anticipatory worry) and RD3 (reward dependence on social attachment) has been found only in adult patients with sleepwalking (Perogamvros *et al.*, 2015) and not in children (current study), we hypothesize that the persistence of sleepwalking in adulthood (2% of the general population compared to up to 13-39% in childhood), may characterize only those individuals with an insecure attachment being added to the ground of an impulsive, unstable and schizotypical profile (which characterizes both child and adult sleepwalking). However, it has to be acknowledged that the JTCI and the TCI differ in terms of scoring and subscales, fact that possible undermine a strict and in-depth comparison between the two groups. Indeed, only HA1 and RD3 subscales (not available in the JCTI) reached statistical significance in adults, but not anticipatory worry (HA) and reward dependence (RD) total scores. Moreover, the Self-Transcendence (ST) scale, which was significantly higher in children compared with their healthy counterpart, mainly reflects the adult Self-forgetful (ST1) subscale, which is the only ST adult subscale that was higher also in the previous study in adults.

Of note, most children and adults who have these sleep disorders do not have a full-blown diagnosis of a psychiatric or personality disorder Indeed, the classical "schizotypal personality style" has been associated with the specific combination of low Self-Directedness, high Self-Transcendence and low Cooperativeness, while Cluster B personality disorders are characterized by high Novelty Seeking, high Harm Avoidance, low RD, low Self-Directedness and low Self-Transcendence (Cloninger, 2002b). On the other hand, people with healthy creative self-awareness, mature creativity and spirituality, score high in all three-character dimensions (Self-Directedness, Cooperativeness, Self-Tracendance, Cloninger and Cloninger, 2013; Cloninger and Zohar, 2011). Therefore, individuals with DOA seem to be characterized by a personality profile that is intermediate between healthy personality development and full-blown mental disorders.

Taken together, these results suggest that: 1) there is a close correspondence between results in the adult and children population of DOA; 2) the main shared features are the presence of high the

Novelty Seeking (NS) and low the Self-Directedness (SD) scales; 3) the described profiles suggest the existence of personality traits associated with DOA, but not of full-blown personality disorders.

These observations have several implications for DOA clinical management and research. First, in neurobiological terms, specific TCI dimensions have been connected to the function of specific brain circuits. In particular, Novelty Seeking reflects high activity within the mesolimbic dopaminergic (ML-DA) system and broadly speaking, reward-seeking brain functions. Second, both temperament and character personality dimensions are strongly heritable (Cloninger et al., 2019; Zwir, Arnedo, et al., 2020b, 2020a; Zwir, Mishra, et al., 2020). Thus, it might be speculated that these personality traits represent not only priming but also predisposing factors and that, when looking at the polygenetic aspects of DOA, future studies should focus not only on immune related features (Lecendreux et al., 2003; Heidbreder et al., 2016), and on slow-wave related (Zadra *et al.*, 2013) or apnea-related genes (Guilleminault *et al.*, 2005), but also on genetic components of human personality (e.g., reward seeking, He *et al.*, 2018). Third, the current study has the advantage to detect personality traits during a period of relative plasticity for the development of personality of an individual (Zohar *et al.*, 2019). This may also have some implications for treatment, as childhood/adolescence may provide an opportunity to tailor personalized psychotherapeutic interventions to prevent the persistence of DOA into the adult life. Insecure social attachment and/or mindfulness training may be useful treatment targets to reduce the outlook of separation characteristic of patients with DOA (Cloninger and Cloninger, 2011).

This work has some limitations to disclose. First, the study is questionnaire-based, and a psychiatric in-depth clinical interview with a specific focus on psychological/psychiatric problems is missing. Second, although the sample size is fairly large with respect to previous studies, larger studies are needed to confirm results using stratified sampling designs to control for potential confounders.

Conclusions

Children and adolescents with DOA exhibit specific psychobiological personality traits compared to age- and gender- matched control subjects. Future research is warranted to evaluate the implications from both a research perspective (genes and circuits implicated) and from a clinical perspective. Indeed, our findings encourage physicians to always explore psychological traits in children and adolescents with a diagnosis of DOA, and suggest potential areas of intervention.

Acknowledgements

We are grateful to all patients and families who participated in the study.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of competing interest

The authors declare no conflicts of interest.

Author contributor-ship: AC and EZ formulated the idea of the study, AC, EZ, AB, AG, PP, MT, recruited patients for the study, AC analyzed data, RCC, LP and AC interpreted data, KT, AC, LP, RCC drafted the paper. All authors revised the draft versions, read and approved the final manuscript.

References

American Academy of Sleep Medicine (2014) *International Classification of Sleep Disorders*. 3rd edn. Darien, IL: American Academy of Sleep Medicine.

Andriola, E. *et al.* (2012) "The Junior Temperament and Character Inventory: Italian validation of a questionnaire for the measurement of personality from ages 6 to 16 years," *Comprehensive Psychiatry*, 53(6), pp. 884–892. doi:10.1016/j.comppsych.2012.01.008.

Arnulf, I. *et al.* (2014) "A scale for assessing the severity of arousal disorders," *Sleep*, 37(1), pp. 127–136. doi:10.5665/sleep.3322.

Berry, R.B. *et al.* (2017) "AASM Scoring Manual Updates for 2017 (Version 2.4)," *Journal of Clinical Sleep Medicine*, 13(05), pp. 665–666. doi:10.5664/jcsm.6576.

Bonkalo, A. (1974) “Impulsive acts and confusional states during incomplete arousal from sleep: Criminological and forensic implications,” *The Psychiatric Quarterly*, 48(3), pp. 400–409. doi:10.1007/BF01562162.

Boyden, S.D., Pott, M. and Starks, P.T. (2018) “An evolutionary perspective on night terrors,” *Evolution, Medicine, and Public Health*, 2018(1), pp. 100–105. doi:10.1093/emph/eoy010.

Bruni, O. *et al.* (1996) “The Sleep Disturbance Scale for Children (SDSC) Construct ion and validation of an instrument to evaluate sleep disturbances in childhood and adolescence,” *Journal of Sleep Research*, 5(4). doi:10.1111/j.1365-2869.1996.00251.x.

Castelnovo, A. *et al.* (2018) “NREM sleep parasomnias as disorders of sleep-state dissociation,” *Nature Reviews Neurology*, 14(8). doi:10.1038/s41582-018-0030-y.

Castelnovo, A. *et al.* (2021) “Behavioural and emotional profiles of children and adolescents with disorders of arousal,” *Journal of Sleep Research*, 30(1). doi:10.1111/jsr.13188.

Cloninger, C. *et al.* (1994) “ The temperament and character inventory (TCI): A guide to its development and use,” in Washington University (ed.). St-Louis, MO.

Cloninger, C.R. (2002a) “Psychobiology and treatment of borderline personality disorder,” *Acta Neuropsychiatrica*, 14(2), pp. 60–65. doi:10.1034/j.1601-5215.2002.140202.x.

Cloninger, C.R. (2002b) “Psychobiology and treatment of borderline personality disorder,” *Acta Neuropsychiatrica*, 14(2), pp. 60–65. doi:10.1034/j.1601-5215.2002.140202.x.

Cloninger, C.R. *et al.* (2019) “The complex genetics and biology of human temperament: a review of traditional concepts in relation to new molecular findings,” *Translational Psychiatry*, 9(1), p. 290. doi:10.1038/s41398-019-0621-4.

Cloninger, C.R. and Cloninger, K.M. (2011) “Person-centered Therapeutics,” *The International Journal of Person Centered Medicine*, 1(1), pp. 43–52. doi:10.5750/ijpcm.v1i1.21.

Cloninger, C.R. and Cloninger, K.M. (2013) “People Create Health: Effective Health Promotion is a Creative Process.,” *International journal of person centered medicine*, 3(2), pp. 114–122. doi:10.5750/ijpcm.v3i2.399.

Cloninger, C.R. and Zohar, A.H. (2011) “Personality and the perception of health and happiness,” *Journal of Affective Disorders*, 128(1–2), pp. 24–32. doi:10.1016/j.jad.2010.06.012.

Dollinger, S.J. (1982) “On the Varieties of Childhood Sleep Disturbance,” *Journal of Clinical Child Psychology*, 11(2), pp. 107–116. doi:10.1207/s15374424jccp1102_3.

Espa, F. *et al.* (2002) “Arousal Reactions in Sleepwalking and Night Terrors in Adults: The Role of Respiratory Events,” *Sleep*, 25(8), pp. 32–36. doi:10.1093/sleep/25.8.32.

Fisher, B.E. and Wilson, A.E. (1987) “Selected Sleep Disturbances in School Children Reported by Parents: Prevalence, Interrelationships, Behavioral Correlates and Parental Attributions,” *Perceptual and Motor Skills*, 64(3_suppl), pp. 1147–1157. doi:10.2466/pms.1987.64.3c.1147.

Gau, S.-F. and Suen Soong, W.-T. (1999) “Psychiatric Comorbidity of Adolescents with Sleep Terrors or Sleepwalking: A Case-Control Study,” *Australian & New Zealand Journal of Psychiatry*, 33(5), pp. 734–739. doi:10.1080/j.1440-1614.1999.00610.x.

Giesbrecht, T. and Merckelbach, H. (2004) “Subjective sleep experiences are related to dissociation,” *Personality and Individual Differences*, 37(7), pp. 1341–1345. doi:10.1016/j.paid.2004.01.004.

Guilleminault, C. *et al.* (2005) “Adult chronic sleepwalking and its treatment based on polysomnography,” *Brain*, 128(5), pp. 1062–1069. doi:10.1093/brain/awh481.

Hartmann E (1989) “Boundaries of dreams, boundaries of dreamers: thin and thick boundaries as a new personality measure,” *Psychiatr J Univ Ott*, 14(4), pp. 557–60.

He, Y. *et al.* (2018) “Candidate genes for novelty-seeking,” *Psychiatric Genetics*, 28(6), pp. 97–109. doi:10.1097/YPG.0000000000000209.

Heidbreder, A. *et al.* (2016) “Not Only Sleepwalking But NREM Parasomnia Irrespective of the Type Is Associated with HLA DQB1*05:01,” *Journal of Clinical Sleep Medicine*, 12(04), pp. 565–570. doi:10.5664/jcsm.5692.

Klackenberg, G. (1982) “Somnambulism in childhood-prevalence, course and behavioral correlations” *Acta Paediatrica*, 71(3), pp. 495–499. doi:10.1111/j.1651-2227.1982.tb09458.x.

Laberge, L. *et al.* (2000) “Development of Parasomnias From Childhood to Early Adolescence,” *Pediatrics*, 106(1). doi:10.1542/peds.106.1.67.

Laidlaw, T.M. *et al.* (2005) “Low self-directedness (TCI), mood, schizotypy and hypnotic susceptibility,” *Personality and Individual Differences*, 39(2), pp. 469–480. doi:10.1016/j.paid.2005.01.025.

Lecendreux, M. *et al.* (2003) “HLA and genetic susceptibility to sleepwalking,” *Molecular Psychiatry*, 8(1), pp. 114–117. doi:10.1038/sj.mp.4001203.

Licis, A.K. *et al.* (2011) “Novel genetic findings in an extended family pedigree with sleepwalking,” *Neurology*, 76(1), pp. 49–52. doi:10.1212/WNL.0b013e318203e964.

Lopez, R., Jaussent, I. and Dauvilliers, Y. (2014) “Objective daytime sleepiness in patients with somnambulism or sleep terrors,” *Neurology*, 83(22), pp. 2070–2076. doi:10.1212/WNL.0000000000001019.

Ohayon, M.M., Guilleminault, C. and Priest, R.G. (1999) “Night Terrors, Sleepwalking, and Confusional Arousals in the General Population,” *The Journal of Clinical Psychiatry*, 60(4), pp. 268–276. doi:10.4088/JCP.v60n0413.

Ohayon, M.M. and Schenck, C.H. (2010) “Violent behavior during sleep: Prevalence, comorbidity and consequences,” *Sleep Medicine*, 11(9). doi:10.1016/j.sleep.2010.02.016.

Oudiette, D. *et al.* (2009) “Dreamlike Mentations During Sleepwalking and Sleep Terrors in Adults,” *Sleep*, 32(12), pp. 1621–1627. doi:10.1093/sleep/32.12.1621.

Perogamvros, L. *et al.* (2015) “Increased Reward-Related Behaviors during Sleep and Wakefulness in Sleepwalking and Idiopathic Nightmares,” *PLOS ONE*, 10(8), p. e0134504. doi:10.1371/journal.pone.0134504.

Perogamvros, L. *et al.* (2020) “Failure of fear extinction in insomnia: An evolutionary perspective,” *Sleep Medicine Reviews*, 51, p. 101277. doi:10.1016/j.smrv.2020.101277.

Petit, D. *et al.* (2007) “Dyssomnias and Parasomnias in Early Childhood,” *Pediatrics*, 119(5), pp. e1016–e1025. doi:10.1542/peds.2006-2132.

Pilon, M., Montplaisir, J. and Zadra, A. (2008) “Precipitating factors of somnambulism: Impact of sleep deprivation and forced arousals,” *Neurology*, 70(24), pp. 2284–2290. doi:10.1212/01.wnl.0000304082.49839.86.

Ramm, M., *et al.* (2020) “Increased behavioral inhibition trait and negative stress coping in non–rapid eye movement parasomnias,” *Clinical Journal of Sleep Medicine*, 16(10), pp. 1737-1744.

Schenck CH *et al.* (1989) “A polysomnographic and clinical report on sleep-related injury in 100 adult patients,” *American Journal of Psychiatry*, 146(9), pp. 1166–1173. doi:10.1176/ajp.146.9.1166.

Schmidt, R.E., Gay, P. and van der Linden, M. (2008) “Facets of Impulsivity Are Differentially Linked to Insomnia: Evidence From an Exploratory Study,” *Behavioral Sleep Medicine*, 6(3), pp. 178–192. doi:10.1080/15402000802162570.

Schredl, M. *et al.* (1999) “Dream content and personality: Thick vs. Thin boundaries.,” *Dreaming*, 9(4), pp. 257–263. doi:10.1023/A:1021336103535.

Simor, P. *et al.* (2011) “Mindfulness and dream quality: The inverse relationship between mindfulness and negative dream affect,” *Scandinavian Journal of Psychology*, 52(4), pp. 369–375. doi:10.1111/j.1467-9450.2011.00888.x.

Smith, M.J. *et al.* (2008) “Temperament and character as schizophrenia-related endophenotypes in non-psychotic siblings,” *Schizophrenia Research*, 104(1–3), pp. 198–205. doi:10.1016/j.schres.2008.06.025.

Stallman, H.M. and Kohler, M. (2016) “Prevalence of Sleepwalking: A Systematic Review and Meta-Analysis,” *PLOS ONE*, 11(11). doi:10.1371/journal.pone.0164769.

Szelenberger, W., Niemcewicz, S. and DĄbrowska, A.J. (2005) “Sleepwalking and night terrors: Psychopathological and psychophysiological correlates,” *International Review of Psychiatry*, 17(4), pp. 263–270. doi:10.1080/09540260500104573.

Zadra, A. *et al.* (2013) “Somnambulism: clinical aspects and pathophysiological hypotheses,” *The Lancet Neurology*, 12(3). doi:10.1016/S1474-4422(12)70322-8.

Zohar, A.H. *et al.* (2019) “The development of temperament and character during adolescence: The processes and phases of change,” *Development and Psychopathology*, 31(02), pp. 601–617. doi:10.1017/S0954579418000159.

Zwir, I., Arnedo, J., *et al.* (2020a) "Uncovering the complex genetics of human character," *Molecular Psychiatry*, 25(10), pp. 2295–2312. doi:10.1038/s41380-018-0263-6.

Zwir, I., Mishra, P., *et al.* (2020) "Uncovering the complex genetics of human personality: response from authors on the PGMRA Model," *Molecular Psychiatry*, 25(10), pp. 2210–2213. doi:10.1038/s41380-019-0399-z.

Zwir, I., Arnedo, J., *et al.* (2020b) "Uncovering the complex genetics of human temperament," *Molecular Psychiatry*, 25(10), pp. 2275–2294. doi:10.1038/s41380-018-0264-5.

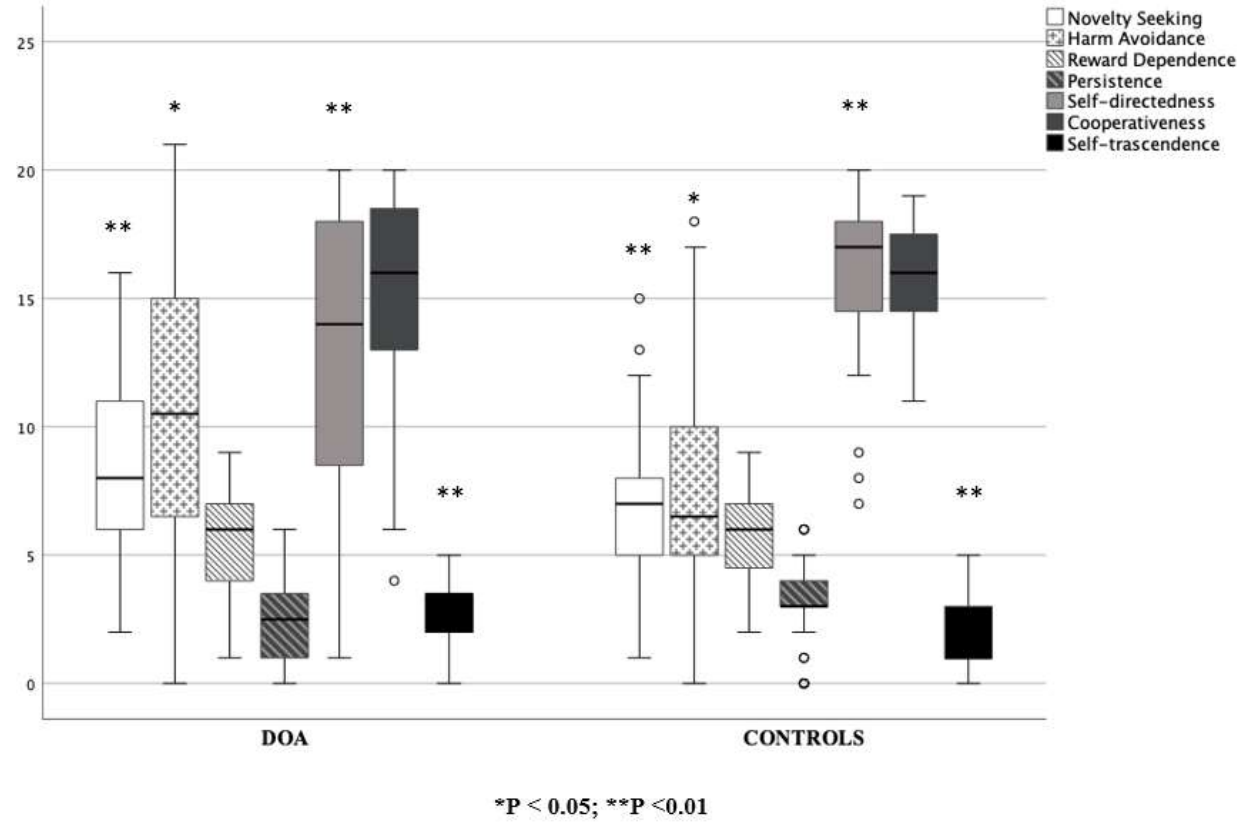
Table 1 PADSS, SDSC and JTCI scores in patients and controls

	DOA GROUP n = 36	**CONTROL GROUP n = 36**	**P-VALUE**	**EFFECT SIZE**
	Mean ± SD	**Mean ± SD**	**p**	**Cohen's D**
PADSS				
Total score	10.94 ± 5.61	0.77 ± 1.82	**<0.0001**	2.56
PADSS-A	5.29 ± 3.50	0.30 ± 0.75	**<0.0001**	2.25
PADSS-B	3.17 ± 144	0.33 ± 0.75	**<0.0001**	2.07
PADSS-C	2.5 ± 1.68	0.14 ± 0.42	**<0.0001**	2.58
SDSC T-SCORE				
Total score	76.0 ± 17.96	50.2 ± 7.79	**<0.0001**	1.09
DIMS	67.7 ± 16.05	52.62 ± 9.25	**<0.0001**	0.95
SBD	60.0 ± 18.35	51.44 ± 5.36	0.01	0.75
DA	80.79 ± 15.3	49.31 ± 5.32	**<0.0001**	1.94
SWTD	70.85 ± 19.22	49.28 ± 8.52	**<0.0001**	1.44
DES	60.67 ± 17.57	48.79 ± 6.11	**0.0005**	0.89
SHY	61.52 ± 15.36	49.13 ± 5.58	**<0.0001**	1.13
JTCI				
Novelty Seeking (NS total)	9.00 ± 3.44	6.38 ± 2.98	**0.005**	0.68
Harm Avoidance (HA total)	10.35 ± 5.17	7.58 ± 4.34	0.01	0.61

Reward Dependence (RD total)	5.81 ± 1.87	5.86 ± 1.88	0.9	-0.03
Persistence (P total)	2.56 ± 1.68	3.27 ± 1.64	0.07	-0.43
Self-directedness (SD total)	12.84 ± 5.73	16.06 ± 3.32	**0.004**	-0.71
Cooperativeness (CO total)	15.21 ± 4.31	15.69 ± 2.2	0.6	-0.15
Self-transcendence (ST total)	2.56 ± 1.32	1.72 ± 1.37	**0.006**	0.66

Legend: DOA: disorders of arousal; PADSS: Paris Arousal Disorder Severity Scale; SDSC: Sleep Disturbances Scale for Children; DIMS: disorders in initiating and maintaining sleep; SBD: sleep breathing disorders; DA: disorders of arousal; SWTD: sleep-wake transition disorders; DES: disorders of excessive somnolence; SHY: sleep hyperhidrosis; JTCI: Junior Temperament and Character Inventory
Statistically significant results are shown in bold characters.

Fig. 1. Personality traits assessed with the JTCI in DOA group vs control group



***P < 0.05; **P <0.01**

Distribution of JTCI score divided between DOA patients and controls (Novelty seeking: P = 0.005; Harm avoidance: P = 0.011; Reward Dependence: P = 0.9; Persistence: P = 0.07; Self-directedness: P = 0.004; Cooperativeness: P = 0.6; Self-transcendenc: P = 0.006).

Legend: JTCI: Junior Temperament and Character Inventory; DOA: disorders of arousal