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A Novel Group Cognitive Behavioural Therapy Approach to Adult Non-Rapid Eye Movement Parasomnias

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The authors declare a potential conflict of interest and state it below

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Two authors wish to make the editor aware of:

1. Professor Allan H Young - Declaration of Interests:

- Employed by King's College London; Honorary Consultant SLaM (NHS UK)
- .Paid lectures and advisory boards for the following companies with drugs used in affective and related disorders: AstraZenaca, Eli Lilly, Lundbeck, Sunovion, Servier, Livanova, Janssen, Allergan, Bionomics, Sumitomo Dainippon Pharma, COMPASS
- Consultant to Johnson & Johnson
- Consultant to Livanova
- Received honoraria for attending advisory boards and presenting talks at meetings organised by LivaNova.
- Principal Investigator in the Restore-Life VNS registry study funded by LivaNova.
- Principal Investigator on ESKETINTRD3004: "An Open-label, Long-term, Safety and Efficacy Study of Intranasal Esketamine in Treatment-resistant Depression."
- Principal Investigator on "The Effects of Psilocybin on Cognitive Function in Healthy Participants"
- Principal Investigator on "The Safety and Efficacy of Psilocybin in Participants with Treatment-Resistant Depression (P-TRD)"
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Conceptualization: DO'R, AN and IR. Methodology and study administration: DO'R, AN, NB, PD, HS, GDL, JS, AB, ID, SH and IR. Drafting and reviewing: all authors.

Keywords

Cognitive behavioral therapy (CBT), NREM parasomnia, Parasomnia, Treatment, therapy

Abstract

Word count: 249

Background: Following the success of Cognitive Behavioral Therapy (CBT) for insomnia, there has been a growing recognition that similar treatment approaches might be equally beneficial for other major sleep disorders, including non-rapid eye movement (NREM) parasomnias. We have developed a novel, group-based, CBT-program for NREM parasomnias (CBT-NREMP), with the primary aim of reducing NREM parasomnia severity with relatively few treatment sessions.

Methods: We investigated the effectiveness of CBT-NREMP in 46 retrospectively-identified patients, who completed five outpatient therapy sessions. The outcomes pre- and post- CBT-NREMP treatment on clinical measures of insomnia (Insomnia Severity Index), NREM parasomnias (Paris Arousal Disorders Severity Scale) and anxiety and depression (Hospital Anxiety and Depression Scale), were retrospectively collected and analyzed. In order to investigate the temporal stability of CBT-NREMP, we also assessed a subgroup of 8 patients during the three to six month follow-up period.

Results: CBT-NREMP led to a reduction in clinical measures of NREM parasomnia, insomnia, and anxiety and depression severities (pre- versus post-CBT-NREMP scores: P (Insomnia Severity Index) =0.000054; P (Paris Arousal Disorders Severity Scale) =0.00032; P (Hospital Anxiety and Depression Scale) =0.037). Improvements in clinical measures of NREM and insomnia severities were similarly recorded for a subgroup of eight patients at follow-up, demonstrating that patients continued to improve post CBT-NREMP.

Conclusion: Our findings suggest that group CBT-NREMP intervention is a safe, effective and promising treatment for NREM parasomnia, especially when precipitating and perpetuating factors are behaviorally and psychologically driven. Future randomized controlled trials are now required to robustly confirm these findings.

Contribution to the field

Over recent years there has been a paradigm shift from pharmacological to non-pharmacological treatment of major sleep disorders, which has been largely driven by the success of Cognitive Behavioural Therapy (CBT) for insomnia. Contemporary publications on non-rapid eye-movement (NREM) parasomnia treatment have bemoaned the lack of a structured CBT intervention, which is viewed as the next milestone in the field (e.g. <https://doi.org/10.1080/00325481.2019.1697119>). We have therefore developed a novel, group-based CBT intervention for NREM parasomnias (CBT-NREMP), and have retrospectively examined its effectiveness in 46 patients, utilizing routinely administered clinical questionnaires. In this brief research paper, we demonstrate that 5 sessions of outpatient group CBT-NREMP results in a clinically meaningful, and statistically significant reduction in NREM parasomnia, insomnia, and anxiety and depression severities. For a subgroup of 8 patients, we additionally demonstrate that these improvements continue post CBT-NREMP. Our findings suggest that group CBT-NREMP intervention is a safe, effective and promising treatment for NREM parasomnia, especially when precipitating and perpetuating factors are behaviorally and psychologically driven. Future randomized controlled trials are required to robustly confirm these findings.

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Studies involving human subjects

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Inclusion of identifiable human data

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Data availability statement

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Key Words: Cognitive Behavioral Therapy (CBT), NREM parasomnia, parasomnia, treatment, therapy

27 **Abstract**

28 **Background:** Following the success of Cognitive Behavioral Therapy (CBT) for insomnia,
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30 beneficial for other major sleep disorders, including non-rapid eye movement (NREM)
31 parasomnias. We have developed a novel, group-based, CBT-program for NREM parasomnias
32 (CBT-NREMP), with the primary aim of reducing NREM parasomnia severity with relatively
33 few treatment sessions.

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35 **Methods:** We investigated the effectiveness of CBT-NREMP in 46 retrospectively-identified
36 patients, who completed five outpatient therapy sessions. The outcomes pre- and post- CBT-
37 NREMP treatment on clinical measures of insomnia (Insomnia Severity Index), NREM
38 parasomnias (Paris Arousal Disorders Severity Scale) and anxiety and depression (Hospital
39 Anxiety and Depression Scale), were retrospectively collected and analyzed. In order to
40 investigate the temporal stability of CBT-NREMP, we also assessed a subgroup of 8 patients
41 during the three to six month follow-up period.

42

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44 and anxiety and depression severities (pre- *versus* post-CBT-NREMP scores: *P* (Insomnia
45 Severity Index) =0.000054; *P* (Paris Arousal Disorders Severity Scale) =0.00032; *P* (Hospital
46 Anxiety and Depression Scale) =0.037). Improvements in clinical measures of NREM and
47 insomnia severities were similarly recorded for a subgroup of eight patients at follow-up,
48 demonstrating that patients continued to improve post CBT-NREMP.

49

50 **Conclusion:** Our findings suggest that group CBT-NREMP intervention is a safe, effective
51 and promising treatment for NREM parasomnia, especially when precipitating and
52 perpetuating factors are behaviorally and psychologically driven. Future randomized controlled
53 trials are now required to robustly confirm these findings.

54

55

56 1. Introduction

57 Non-Rapid Eye Movement (NREM) parasomnias, or arousal disorders, are common in adults,
58 where they represent a constellation of different unwanted behaviors and experiences, arising
59 from or associated with sleep, for example from sleep walking to sexsomnia (Ito and Inoue
60 2015). In addition to night-time symptoms, they can also result in next day excessive tiredness,
61 as well as adversely affect mood, cognition, and quality of life (Singh et al. 2018). Genetic
62 predisposition plays a role and it is most evident in sleepwalking (Rodriguez and Foldvary-
63 Schaefer 2019). Arousal disorders can be an important cause of sleep-related injury (Ingravallo
64 Francesca et al. 2014; Arnulf et al. 2014), and it is crucial that their severity can be reliably
65 diagnosed and assessed. More recently, Arnulf and colleagues (2014) developed the Paris
66 Arousal Disorders Severity Scale (PADSS), which has been consistently demonstrated across
67 different NREM parasomnia phenotypes to reliably monitor and measure the clinical
68 symptoms and severity of arousal disorders (Arnulf et al. 2014).

69 The understanding of the exact neurobiology and the maladaptive arousal mechanisms that
70 underlie phenotypes of NREM parasomnia remains in its infancy (Gnoni et al. 2020; Ramm et
71 al. 2020; Rodriguez and Foldvary-Schaefer 2019; Rocha and Arnulf 2020; Drakatos and
72 Leschziner 2019). Management is commonly multifaceted with an emphasis on
73 psychoeducation and ideally on non-pharmacological measures (Rodriguez and Foldvary-
74 Schaefer 2019). Pharmacotherapy is nonetheless frequently used in the treatment of NREM
75 parasomnias (Drakatos et al. 2019). However, it is not always effective or wanted by patients,
76 often because of fear of side-effects and dependency (Rodriguez and Foldvary-Schaefer 2019).
77 Treatment success rates vary between different NREM parasomnia phenotypes, and
78 polypharmacy may be required (Drakatos et al. 2019). In some cases, certain treatments, such
79 as antidepressants, can worsen or even precipitate parasomnia symptoms (Stallman, Kohler,
80 and White 2018). As NREM parasomnias are often chronic conditions, pharmacological
81 treatment may be required long-term, which is often undesirable, especially when the patient
82 is a young adult. Even when pharmacotherapy is successful, NREM parasomnias can re-
83 emerge following treatment cessation, particularly if priming and precipitating factors remain
84 unaddressed (Howell 2012).

85 **Of note is that affective disorders, and especially anxiety disorder, may lead to an increased**
86 **frequency of negative emotions in NREM parasomnia mentation, and that this in turn may**
87 **further increase daytime anxiety (de Macêdo et al. 2019). Moreover, it has been argued that the**
88 **reported distress associated with parasomnia/nightmare experience may have a more**
89 **significant impact on patients' quality of life, even more so than the frequency of parasomnic**
90 **events (for an in-depth review of this topic please refer to de Macêdo et al. 2019). In keeping**
91 **with this, to date, several psychotherapeutic approaches, for example: via Gestalt therapy**
92 **(Holzinger, Klösch, and Saletu 2015) and imagery rehearsal therapy (Stefani and Högl 2020),**
93 **have been shown to successfully target dysphoric parasomnias and to treat associated**
94 **significant clinical distress.**

95 In order to address the growing need for non-pharmacological therapies for NREM
96 parasomnias (Galbiati et al. 2015), we have recently developed a novel, group-based, Cognitive
97 Behavioral Therapy (CBT-NREMP) programme. The pathophysiological precipitants of
98 NREM parasomnias suggest that CBT interventions, which address co-morbid insomnia,
99 anxiety, stress and other relevant psychological difficulties, may be beneficial in its
100 management (Pressman 2007). Our goal was therefore to primarily target factors which may
101 trigger and maintain parasomnias over time, by incorporating and building-on core principles
102 from the well-established and **cost-effective (Tolin 2010) Cognitive Behavioral Therapy for**

103 Insomnia (CBT-I) (Perlis et al. 2005). The novel CBT for NREM parasomnia (CBT-NREMP;
104 [Supplement](#)) protocol includes a comprehensive programme that covers psychoeducation on
105 the etiology of NREM parasomnias, sleep hygiene, sleep rescheduling to optimize homeostatic
106 regulation, stimulus control to re-establish an association between the bed/bedroom and sleep,
107 and specified body-based and cognitive relaxation techniques. By changing maladaptive sleep-
108 related behaviours, thoughts and anxiety, CBT-NREMP treatment is specifically designed to
109 target those priming and precipitating factors which cause parasomnias to persist over time.
110 Moreover, it enables an individual to gain insight into their own thoughts as well as their
111 emotional and behavioral processes regarding the self. The CBT programme is delivered in a
112 safe group environment that additionally utilizes the spontaneity and creativity of the individual
113 and the group. Here we report on the preliminary treatment outcomes of our novel CBT-
114 NREMP programme.

115

116 **2. Materials and methods**

117 **2.1 Design, Ethics and Data Collection**

118 All adult patients who had completed a whole programme (i.e. five sessions) of a structured
119 group CBT-NREMP between November 2018 and January 2020 were retrospectively
120 identified, and their clinical findings, including demographics and the scores of several clinical
121 questionnaires routinely used in our service, were collected from the clinical sleep database at
122 the tertiary sleep centre, and analysed. Altogether forty-six patients were identified matching
123 that criteria, and of those, a subgroup of eight patients were identified for whom three to six
124 months follow up assessment findings were also available ([Figure 1](#)).

125 As per our clinical governance, the specified requirements to enrol in CBT-NREMP included
126 a conducted video polysomnography (vPSG) investigation, and a confirmed diagnosis of
127 NREM parasomnia by a qualified sleep physician, based on International Classification of
128 Sleep Disorders third edition (ICSD-3) criteria (Ito and Inoue 2015). In addition to these
129 inclusion criteria, all referred patients were screened by an experienced
130 psychiatrist/psychologist, to confirm and assess their ability to participate in the group
131 psychotherapy, as well as to ascertain the patient's ability to understand, speak and write
132 English language, and to confirm their willingness and ability to give informed consent. The
133 CBT-NREMP exclusion criteria included: co-morbid sleep disorders (apart from comorbid
134 insomnia), current or past neurologic or psychiatric illness, traumatic brain injury, current
135 alcohol and/or substance dependency disorders, developmental disorders and intellectual
136 disability.

137 For the purposes of this study, the effectiveness of CBT-NREMP was evaluated by analysing
138 the outcomes of the three major clinical questionnaires from the clinical sleep database,
139 including the Insomnia Severity Index (ISI) (Bastien, Vallières, and Morin 2001), Hospital
140 Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983), and the Paris Arousal
141 Disorder Severity Scale (PADSS) (Arnulf et al. 2014) at baseline, post-CBT-NREMP, and at
142 follow-up (FU) three to six months later.

143 ISI is a self-rated scale, used to assess severity of insomnia in the clinical and research settings
144 (Morin et al. 2011). The scale uses a seven-item self-report questionnaire that examines the
145 nature, severity, and impact of insomnia. The evaluated dimensions include severity of sleep
146 onset, sleep maintenance, and early morning awakening problems, sleep dissatisfaction,

147 interference of sleep difficulties with daytime functioning, noticeability of sleep problems by
148 others, and distress caused by the sleep difficulties. A five-point Likert scale is used to rate
149 each item (e.g., 0 = no problem; 4 = very severe problem), yielding a total score ranging from
150 0 to 28 (Morin et al. 2011). Based on the total score the absence of insomnia (0–7); sub-
151 threshold insomnia (8–14); moderate insomnia (15–21); or severe insomnia (22–28) can be
152 identified (Bastien, Vallières, and Morin 2001). Similarly, HADS is also a self-rated scale, used
153 to assess severity of depression and anxiety symptomatology (Zigmond and Snaith 1983). This
154 fourteen-item scale includes seven items each for anxiety and depression subscales, where
155 scoring for each item ranges from zero to three. A subscale score >eight denotes anxiety or
156 depression. PADSS is a self-administered questionnaire designed to assess the severity of
157 parasomnia (Arnulf et al. 2014). The scale has excellent psychometric properties, as well as
158 valid and reliable subscales (Hrozanova, Morrison, and Riha 2019). It provides a means to
159 assess the efficacy of new intervention treatments, as well as changes over longer periods of
160 time. It consists of 17 items related to severity of parasomnia, with total score ranges from 0 to
161 50 (Arnulf et al. 2014); the scale has three parts, including an inventory of behaviors (PADSS-
162 A), the frequency of episodes (PADSS-B), and the general consequences of the disorder
163 (PADSS-C). The scale is self-completed and measured as follows: dangerous behaviors (17
164 items with three possible answers: never = 0, sometimes = 1, often = 2), frequency of episodes
165 (equal to or more than two episodes per night = 6, one per night = 5, equal to or more than 1
166 episode per week = 4, equal to or more than 1 episode per month = 3, equal to or more than 1
167 episode per year = 2, less than 1 episode per year = 1, never had any = 0), and consequences
168 of the disorder (5 items with three response options: never = 0, sometimes = 1, often = 2). The
169 best cutoff score for the overall PADSS (range 0-50) was found at 13/14 and had high
170 sensitivity (83.6%) and specificity (87.8%) (Arnulf et al. 2014). It has been shown in the past
171 that the complexity of behaviors emerging from N3 sleep as assessed by the vPSG correlate
172 positively with the scores for the PADSS-total, PADSS-A, and PADSS-C (Arnulf et al. 2014;
173 Hrozanova, Morrison, and Riha 2019).

174 The study was granted an ethical approval by the Hospital Clinic Research Ethics Committee
175 (Project-No-12025, GSTT NHS, UK) to retrospectively ascertain anonymized data in full
176 compliance with the EU General Data Protection Regulation and the Declaration of Helsinki.

177 **2.2 CBT-NREMP Treatment**

178 The structured group CBT programme consisted of five, weekly, 90-minute CBT sessions, with
179 a maximum of eight participants per group. CBT-NREMP was conducted by an experienced
180 sleep medicine psychiatrist or a trained psychologist according to a strict predetermined
181 treatment protocol. Our protocol provided therapists with clear guidance on how to structure
182 their therapy, as laid out in [Supplementary Methods](#). The first sessions focused on building a
183 therapeutic alliance and psychoeducation. The interventions sessions focused on both short-
184 and long-term goals. Different cognitive and behavioural techniques ([Supplement](#)) were
185 applied to reach these goals. Homework was given in each session with the last session of
186 therapy focusing on consolidation and relapse prevention. Experienced CBT-clinicians
187 monitored adherence to the treatment principles in weekly group supervisions throughout the
188 therapy period to ensure treatment fidelity. Clinical notes from the therapy sessions were
189 regularly reviewed during supervisory sessions with focus on the initial phase of treatment,
190 case formulation, treatment strategy and termination of therapy.

191 **2.3 Statistical Analyses**

192 Descriptive statistics were used to summarize the data as mean \pm standard deviation (SD), and
193 with median, 25th and 75th percentiles for continuous non-parametric variables. **Due to non-**
194 **normality of the data, as assessed by Kolmogorov-Smirnov test, the non-parametric** Wilcoxon
195 signed rank test (paired comparisons) with Holm-Bonferroni corrections was used (Arnulf et
196 al. 2014; Siegel 1956) to test difference in severity between the CBT-NREMP group's
197 insomnia (i.e. ISI), parasomnia (i.e. PADSS) and depressive and anxiety symptomatology (i.e.
198 HADS) pre- and post-CBT scores. In addition, *post hoc analyses* were done for differences
199 across the three time points, at the baseline, immediately following the CBT-NREMP and at
200 the three to six months follow up (i.e. pre-, post-, and FU-CBT) for eight participants for whom
201 follow-up data were available. A value of $P < 0.05$ was considered to be statistically significant
202 and Holm-Bonferroni corrections were performed for the post-hoc analyses. The analyses were
203 done using a statistical package R, version 4.0.2 for all statistical analyses (Wickham et al.
204 2019).

205 3. Results

206 Forty-six patients, of whom 25 were male (54.3%), aged 19 to 73 years-old (mean \pm SD: 35.8
207 \pm 11.4 years) underwent a structured, comprehensive five weeks CBT-NREMP group
208 intervention. Patients were asked to complete baseline ISI, HADS, and PADSS assessments
209 prior to starting CBT-NREMP, and the same assessments were subsequently completed after
210 the CBT-NREMP intervention (Tables 1, 2).

211
212 At the baseline, patients' PADSS scores reflected the clinical severity of their untreated NREM
213 parasomnia (mean PADSS score: 19.46 \pm 6.32; Table 1). Patients scored moderately high on
214 clinical measures of insomnia (ISI: 15.28 \pm 4.36), with the baseline HADS outcome scores
215 suggestive of subthreshold levels of anxiety and low mood (HADS-A: 8.14 \pm 4.84 *versus*
216 HADS-D: 7.02 \pm 4.05).

217
218 The CBT-NREMP intervention successfully reduced measures of clinical severity of NREM
219 parasomnia (PADSS: $P_{\text{PrevsPost}}=0.00032$; Table 2). Further significant improvements were noted
220 in clinical measures of insomnia (ISI_{PrevsPost}: $P=0.000054$; Table 2), which were reduced to clinical
221 subthreshold values (Table 1), as well as in patients' self-reported severity of anxiety and
222 depressive symptoms (HADS_{PrevsPost}: $P=0.037$; Table 2).

224 3.1 Preliminary findings on sustainability of the CBT-NREMP intervention

225
226 A subgroup of eight patients (17.4%) was followed after the CBT-NREMP intervention for up
227 to six months (please also see Supplementary Results). By comparison to the socio-
228 demographics of the larger group, the smaller subgroup consisted of younger (29.5 \pm 8.1 years),
229 predominantly female (six, 75 %) patients, who at the outset reported higher clinical measures
230 of severity of NREM parasomnia (PADSS scores: 24.75 \pm 3.62; Supplement, Table S1) and
231 anxiety (HADS-A: 11.25 \pm 5.18; Table S1).

232
233 Here, the CBT-NREMP intervention also significantly reduced the clinical measures of
234 severity of NREM parasomnia and insomnia (Table S2); these improvements were
235 maintained, with further reduction in clinical measures of frequency and severity for NREM
236 parasomnia and insomnia reported to continue for up to six months following the intervention
237 (ISI: $P=0.042$; PADSS: $P=0.041$; Table S2).

238

239 The CBT-NREMP intervention, however, did not lead to a statistically significant reduction in
240 clinical measures of low mood and anxiety for this subgroup (HADS: $P=0.22$). Nonetheless,
241 the longitudinal reduction in the mean HADS scores was recorded across the assessment time-
242 points (HADS *Pre*: 17.5 ± 8.64 ; *Post CBT-NREMP*: 14.88 ± 4.52 ; *F/U three to six*
243 *months*: 11.88 ± 7.02 ; [Table S1](#)), with the most consistent improvement reported to occur during
244 the follow up period of up to six months after the intervention (HADS-A: $P=0.057$; [Table S2](#)).
245 This may suggest a delayed nature of this response, or its secondary development on the back
246 of primary improvements in sleep measures.

247 **4. Discussion**

248 The findings of our longitudinal study support the clinical utility for a novel CBT-NREMP
249 intervention that targets distinct sleep, behavioral and emotional regulation factors. More
250 specifically, we demonstrate that five weeks of a structured group CBT intervention in adult
251 patients with NREM parasomnia can lead to a significant reduction in its severity. This is
252 shown by a robust reduction in total PADDs and PADDs-A patients' scores ([Table 1](#)), both
253 known to closely correlate with vPSG-ascertained severity (and complexity) of parasomnia
254 behaviors that emerge from N3 sleep (Arnulf et al. 2014; Hrozanova, Morrison, and Riha
255 2019).

256 In addition, we demonstrate that CBT-NREMP intervention can simultaneously lead to a
257 clinically significant reduction in the patients' severity of insomnia, as evidenced by the
258 reduction in the ISI scores. In our study, the ISI scores were robustly reduced from moderate
259 to subthreshold values, with concomitant improvement in affective symptomatology ([Table](#)
260 [1](#)).

261 We also demonstrate that the effects of CBT-NREMP can be maintained, and that they continue
262 to improve over a period of up to six months following the intervention ([Supplement Table](#)
263 [S2](#)). To the best of our knowledge, our study is the first to demonstrate the effectiveness, and
264 arguably also the safety, of a structured CBT for adult NREM parasomnia.

265 Utilizing CBT in the treatment of sleep disorders holds substantial promise, and is clinically
266 expanding (Bhattarai and Sumerall 2017). Where once medication-only treatments were
267 favoured, there has recently been a paradigm shift towards CBT-based interventions, which are
268 viewed more favorably by patients (Vincent and Lionberg 2001), and treatment guidelines
269 (Wilson et al. 2019). CBT for insomnia (CBT-I) is already well-established as the gold-
270 standard treatment, and principally operates by reducing perpetuating and precipitating factors
271 associated with the condition (Riemann et al. 2017). NREM parasomnias similarly manifest
272 with priming (e.g. sleep loss, anxiety, stress, poor sleep hygiene), and precipitating factors (e.g.
273 environmental noise) (Pressman 2007). Therefore, they should be amenable to a targeted CBT
274 intervention, as our study amply demonstrates. Treating NREM parasomnias with CBT-
275 NREMP, as opposed to medication, may have a number of potential advantages, including
276 fewer known side-effects, and an explicit focus on treating the factors that may be responsible
277 for perpetuating parasomnias in an effort to produce more durable effects.

278 Despite this, the body of literature on cognitive and behavioral interventions for NREM
279 parasomnia is limited to case reports or smaller case-series, which often target just one
280 parasomnia phenotype (Ntafouli et al. 2020). In the past, selective application of CBT-I,
281 mindfulness-based stress reduction and CBT for stress have been shown to helpfully target all
282 phenotypes of NREM parasomnias (Drakatos et al. 2019). In our experience, patients with
283 NREM parasomnia commonly struggle to benefit from other CBT paradigms, where they often
284 feel apart from the rest of the group. For example, it can be understandably challenging for a

285 patient with sleepwalking to engage in, and accept, a therapy which solely focuses on
286 insomnia. Indeed, the development of our targeted group CBT-NREMP arose in part from this
287 unmet patient need.

288 Despite striking and sustainable improvement reported by our patients, several notable
289 limitations merit further mention. Firstly, CBT-NREMP was designed as an economical and
290 inclusive group intervention, which could be potentially delivered in a variety of clinical
291 settings and that reliably targets diverse physiologic phenotypes of arousal disorders. Whilst
292 this was beyond the scope of our study, future studies should ideally examine whether taking
293 a stepped-care approach would be more beneficial for different settings or NREM parasomnia
294 phenotypes, possibly avoiding any potential selection bias. For example, any such multifaceted
295 CBT-NREMP intervention could arguably start with group therapy sessions that address
296 common therapeutic targets in parasomnia (e.g. safety, sleep hygiene), with subsequent
297 individual interventions focusing on specific and more complex phenotypes, such as trauma-
298 related presentations and sexomnia.

299 Secondly, whilst the findings of our study suggest that a robust short term (e.g. three to six
300 months) maintenance of CBT-NREMP effects is possible, this effect was only shown in eight,
301 as opposed for 46 original study patients, due to unforeseen and early study closure during the
302 Covid-19 pandemic. This smaller subgroup had a widely differing sociodemographic in that
303 the patients were notably younger, they reported higher baseline anxiety, and they were
304 predominantly women. Hence, the CBT-NREMP sustainability should be confirmed in a larger
305 patient cohort, and the specific CBT-NREMP effects and their sustainability ideally recorded
306 over a significantly longer period of time.

307 Another potential limitation worth mentioning is that our assessment was based primarily on
308 patients' subjective reports. The self-reported scores, recorded in PADSS, ISI and HADS
309 questionnaires are, however, widely used, and all three have been robustly validated for clinical
310 and research purposes (Morin et al. 2011; Arnulf et al. 2014; Turon et al. 2019). Nonetheless,
311 the subjective nature of patients' reports may arguably render any truly objective interpretation
312 of CBT-NREMP's effectiveness invalid. We challenge the clinical significance of this
313 limitation, given that the major aim of any clinical treatment of NREM parasomnia is primarily
314 offered to ensure patients' safety, and secondly, to address the patients' symptoms according
315 to their own criteria (Drakatos et al. 2019).

316 Taken together, the findings of our study demonstrate that structured group CBT for adult
317 NREM parasomnia is a safe, effective, and a highly promising treatment. Due to its unique
318 design, CBT-NREMP intervention may be especially effective in those patients in whom
319 precipitating and perpetuating factors are likely behaviorally and psychologically driven.
320 However, in order to reliably build on our preliminary study, future randomized controlled
321 trials are required. Ideally, any such trial should include prospective multimodal physiologic
322 and neuroimaging investigation to decipher neuromechanisms which underlie and promote
323 differential effects of CBT-NREMP's intervention. Following this approach, it is hoped that
324 with time we will also gain further insight into the role that patients' gender and their emotional
325 fragility may play. Going forward, it would be important to understand how they may impact
326 objective CBT-NREMP outcomes, including the electroencephalographic arousal signatures
327 and their behavioral correlates.

328 **5 Conflict of Interest**

329 The authors declare that the research was conducted in the absence of any commercial or
330 financial relationships that could be construed as a potential conflict of interest.

331 **6 Author Contributions**

332 Conceptualization: DO'R, AN and IR. Methodology and study administration: DO'R, AN,
333 NB, PD, HS, GDL, JS, AB, ID, SH and IR. Drafting and reviewing: all authors.

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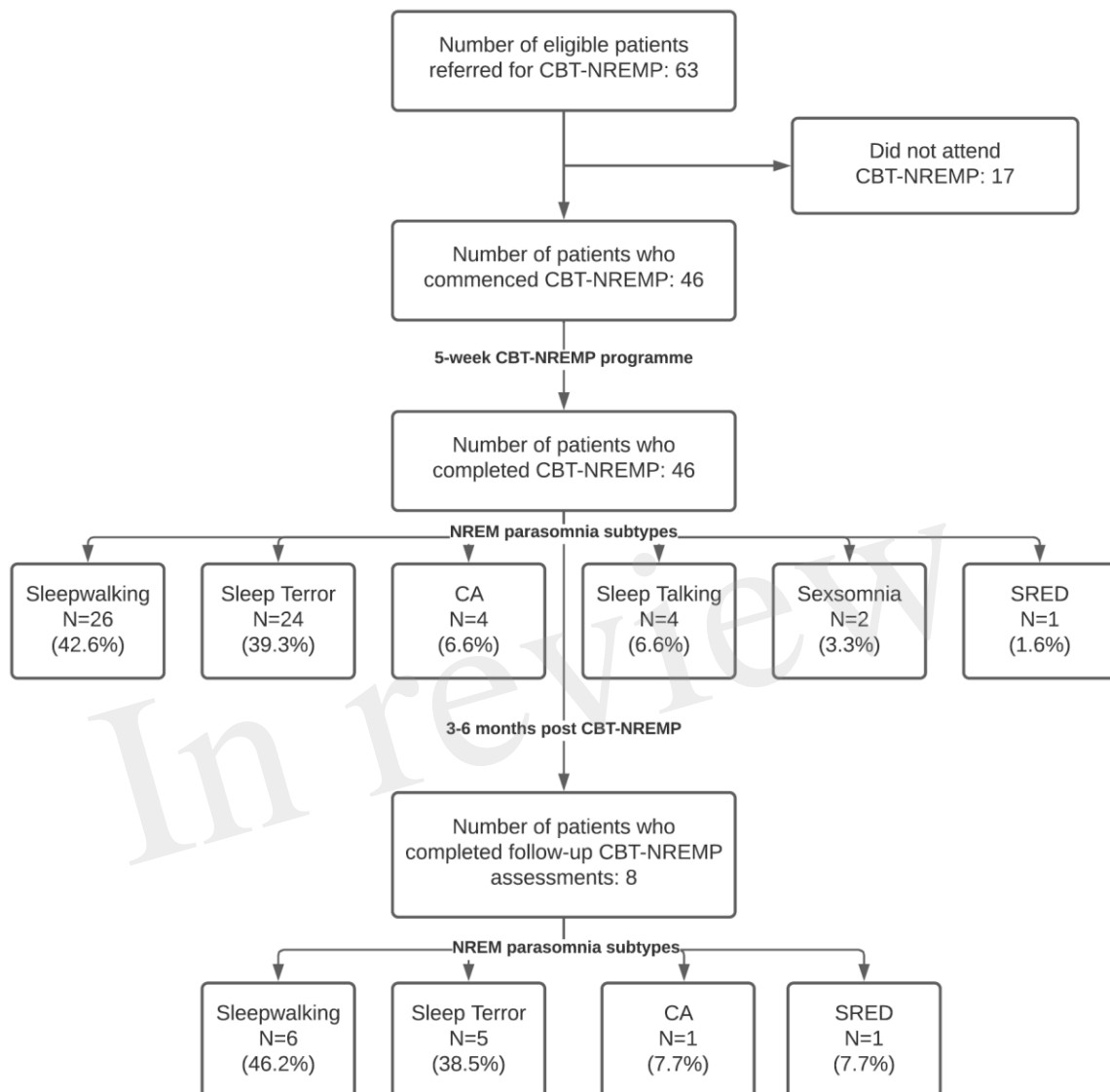
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421

422 **Figures**

423 **Figure 1 Flow diagram of the studied cohort**



424

425 *Nota Bene:* some patients had $n > 1$ subtype of NREM parasomnia recorded. *Abbreviations:*
426 Percentages indicate the prevalence of each NREM parasomnia subtype in our cohort. CBT-
427 NREMP, cognitive behavioral therapy for non-REM parasomnia; CA, confusional arousal;
428 SRED, sleep-related eating disorder; NREM, non-REM; n, number.

429

430

431 **Tables**432 **Table 1** Outcomes of ISI, HADS and PADSS assessments in 46 NREM parasomnia
433 patients at baseline (Pre) and following the CBT-NREMP treatment (Post)

Assessment	Pre		Post	
	Mean (SD)	Median (Q1, Q3)	Mean (SD)	Median (Q1, Q3)
ISI	15.28 (4.36)	15 (12.25, 18)	12.09 (4.6)	12 (9.25, 15)
HADS	15.18 (6.55)	16 (11, 19)	13.13 (5.98)	13 (8, 17.75)
HADS-A	8.14 (4.84)	7 (4.75, 12)	7.22 (4.24)	7 (4, 9.75)
HADS-D	7.02 (4.05)	6 (4, 10)	5.91 (3.74)	6 (3, 9)
PADSS	19.46 (6.32)	19 (16, 23.75)	17.53 (6.11)	17 (14, 22)
PADSS-A	9.8 (4.67)	10 (6.25, 13.5)	8.41 (4.16)	8 (5, 10)
PADSS-B	4.41 (1.11)	4 (4, 5)	4.46 (1.21)	4 (4, 5.75)
PADSS-C	5.24 (1.78)	5 (4, 7)	4.84 (2.01)	5 (3, 6.25)

434

435 *Abbreviations:* ISI, Insomnia Severity Index; HADS, Hospital Anxiety and Depression Scale
436 (total score); HADS-A, Hospital Anxiety and Depression Scale-Anxiety subset score; HAD-
437 D, Hospital Anxiety and Depression Scale - Depression subset score; PADSS, Paris Arousal
438 Disorder Scale (total score); PADSS-A, Paris Arousal Disorder Scale-subset A score; PADSS-
439 B; Paris Arousal Disorder Scale subset-B score; PADSS-C, Paris Arousal Disorder Scale
440 subset-C score. Q1, 25% percentile. Q3, 75% percentile. SD, standard deviation.

441

442

443 **Table 2.** Results of Wilcoxon signed rank tests comparing pre- and post-CBT-NREMP
444 intervention scores for ISI, HADS, and PADSS assessments in 46 NREM parasomnia
445 patients.

446

Assessment	Difference from Pre- to Post-CBT Median (Q1, Q3)	Difference in Median (95% CI)	Wilcoxon signed rank test	P-value
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ISI	3 (0, 6.75)	3 (1, 6)	710.5	0.000054
HADS	1 (-1, 6)	3 (-0.84, 5.84)	514.5	0.037
HADS - A	1 (-1, 3)	0 (-1, 2.97)	512	0.089
HADS - D	1 (0, 2)	0 (-2, 3.5)	467.5	0.034
PADSS	1 (0, 3)	2 (-1.40, 6)	560	0.00032
PADSS – A	1 (-0.75, 2.75)	2 (0, 3.5)	600.5	0.003
PADSS - B	0 (0, 0)	0 (-1, 1)	71.5	0.826
PADSS - C	0 (-0.25, 1)	0 (-1, 2)	306.5	0.119

447

448 *Abbreviations: ISI, Insomnia Severity Index; HADS, Hospital Anxiety and Depression Scale;*
449 *PADSS, Paris Arousal Disorder Scale. Q1, 25% percentile. Q3, 75% percentile. CI,*
450 *confidence interval. CBT, cognitive behavioral therapy. Statistically significant values are*
451 *shown in bold.*

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Figure 1.JPEG

