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Tesi di laurea:

ANALYSIS AND DEVELOPMENT OF A TELEREHABILITATION SYSTEM FOR PEOPLE WITH PARKINSON'S DISEASE BASED ON WEARABLE DEVICES

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ABSTRACT

Parkinson's disease (PD), described firstly by James Parkinson in his 1817 publication, Essay on the Shaking Palsy, is a complex and progressive neurodegenerative disease.

Two hundred years later, neuroprotective therapy for PD has not been definitively achieved. However, the treatment of Parkinson's disease has made considerable progress, in which new treatments and treatment combinations are compared to standard therapy.

The medical department of the Università Politecnica Delle Marche, in partnership with the Revolt srl company, and the University of Verona, with the project RAPIDO, will develop a high complexity integrated system for telerehabilitation and telemonitoring of Parkinson's patients. The expected result is the system development to support the rehabilitation management of the PD in distinct stages of the disease, in the long term, reliable, feasible, economically sustainable, and accessible in residential care.

The purposes of this experimental dissertation are first to describe the technical aspects of the telerehabilitation protocol and the data acquisition infrastructure; then, a statistical analysis method is proposed to quantify the variation of some physiological variables throughout the rehabilitation training.

PD consists of the degeneration of dopaminergic neurons in the NS and protein aggregates within neurons called Lewy bodies and Lewy neurites. However, recent studies have shown that, unlike the loss of neurons in the NS, the loss of dopaminergic terminals in the basal ganglia is essential for developing motor symptoms. Physiotherapists can use manipulations and exercises to relieve muscle stiffness and joint pain. Physical therapists aim to promote movement and improve gait and flexibility. They also try to improve the health of patients and their ability to manage things on their own. Drugs could be administered to improve the main symptoms of PD, such as tremors and movement problems. The problem is that not all available drugs are helpful for everyone; moreover, each drug's short-term and long-term effects are different. There are three commonly used drugs: Levodopa, Dopamine agonist and Monoamine-oxidase B inhibitor. Regular Exercise relieves muscle stiffness, improves mood, and relieves stress. Patients can perform many activities to stay in shape, from more active sports such as tennis and cycling to less strenuous activities such as walking, gardening, and yoga.

In addition, a balanced diet that includes all food groups can provide the body with the nutrients it needs to stay healthy.

As the illness progresses, neurodegenerative disease is characterized by a continuous decline in motor and/or cognitive function, making the journey to the clinic stressful and difficult for patients and caregivers. In addition, lack of adequate transportation, being in rural areas, and limited financial resources can exacerbate the problem. As a result, patient-physician contact becomes very difficult in care, monitoring, and intervention.

Therefore, telemedicine and telehealth approaches can be valuable to address this challenge, especially in this scenario. Telemedicine, by definition, is the dissemination of health-related services using electronic technology, which can improve the continuity of care for patients with Parkinson's. Telemedicine comprehends the remote delivery of health care services. Quantitative evaluation using wearable devices can provide continuous, objective, and environmentally sound data collection. It can be applied frequently at short intervals outside the clinic to track symptom changes in real-time. This approach can also improve patient-physician interactions, influence treatment decisions, and improve patients' overall health.

The experimental study, named RAPIDO *teleRiabilitazione per i mAlati di Parkinson In qualsiasi staDiO*, involves patients affected by Parkinson's disease at any stage in a telerehabilitation process that lasts for three months. For the delivery of the devices, each patient went to the *Ospedali Riuniti* in Ancona, where he was subjected first to the medical team examination and then had an interview with the technical team. Each patient received detailed instructions on using the devices provided to complete the trial successfully.

The first group made of five patients was enlisted to test the entire infrastructure and received: a Samsung A7 tablet that acts as the edge/fog computing node of the local subsystem and that can be used to navigate the web application with rehabilitation therapies, and a Garmin Vivosmart 4 smartwatch that works as a fitness tracker. All data recorded are stored on the Garmin servers and then sent to the remote server through an HTTP POST request. The summary data obtained via push notifications are: Daily summaries that offer a high-level view of the user’s entire day; epoch summary records contain much of the same data available in Daily summaries but with 15-minute time-slice granularity. Stress Details summaries contain the user's stress level values for a given day. Sleep summaries are data records representing how long the user slept and the automatically classified sleep levels during that sleep event (e.g., light, deep periods) based on data generated by the user's device.

The data of the first week of acquisition let to know the pre-training values of each subject. For each of the five patients, four DataFrames were created, one for each group of data summaries recorded. Then a first visual analysis and preprocessing are performed on the data, which allows starting to recognize some patterns, or observing the total sum of days allows understanding how many days the subject has worn the watch compared to the amount of time passed since delivery.

The one-way analysis of variance (ANOVA) is performed to determine if the means of three or more independent (unrelated) groups differ statistically. In our case, the distinct groups represent the different weeks of the rehabilitation process. The one-way ANOVA compares the means between the groups under examination and determines whether those means are statistically significantly different from each other (p-value < 0.05). This method helps to understand, both graphically and numerically, which is the health parameter evolution over time. It is possible to observe if the recorded values move, through the rehabilitation session, to a healthier condition.

Even with little data, and few participants, this pilot study gives an idea of different approaches to rehabilitation. One patient has completed all the rehabilitation sessions in the scheduled time, three are a little behind schedule, and one did not perform any sessions. It was seen that the subject that has already attended almost half of his program reached the most relevant changes in his health status.

Albeit faint and yet to be confirmed with the study of a larger sample of patients who have completed the three months of telerehabilitation, this may be hoped that the proposed clinical study may gain clinical relevance and that, therefore, telerehabilitation can be incorporated into patients' daily therapies.

This work is only the first step in bringing the study closer to application in daily practice; a great deal of future work is needed.

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INTRODUCTION

Parkinson's disease (PD), described firstly by James Parkinson in his 1817 publication, *Essay on the Shaking Palsy* (1), is a complex and progressive neurodegenerative disease. Dr Parkinson affirmed that *there appears to be sufficient reason for hoping that some remedial process may ere long be discovered, by which, at least, the progress of the disease may be stopped.* About fifty years later, Jean-Martin Charcot, a French neurologist and professor of anatomical pathology recognized the importance of Parkinson's discovery and renamed the disorder *Maladie de Parkinson* (Parkinson's disease) (2–4). For years, many scientists have made contributions to the description of the motor and non-motor features, neuropathological, neurochemical, neurophysiological, and neuroimaging characteristics of PD (2). More than two hundred years later, a neuroprotective therapy for PD has not been definitively achieved.

However, much progress has been made to understand the molecular basis of the neurodegeneration of Parkinson's disease, hoping to achieve regulatory therapy for PD. Over the past twenty years, has been made substantial improvement in identifying the genetic basis of PD, especially monogenic disease-causing genes. Although 15% of PD patients have a family history and 5–10% of PD patients suffer from a monogenic form of the disease with Mendelian inheritance, the majority of PD cases are sporadic with unknown aetiology, possibly caused by an association of genetic, environmental and risk factors (5,6).

As the second most spread neurodegenerative disease after Alzheimer's disease (AD), the prevalence of PD is approximately 1% of the individuals over age 60 years and 4% of the population older than age 85 (7).

Pathologically, PD is defined as a loss of dopaminergic neurons in the substantia nigra pars compacta (NS) located in the midbrain and associated with Lewy bodies, which are cytoplasmic inclusions that include insoluble α-synuclein aggregates. However, PD is characterized by more widespread pathology in other brain regions and involves non-dopaminergic neurons. Clinical diagnosis of PD is based primarily on motor functions such as slow progressive asymmetric resting tremors, cogwheel rigidity, and bradykinesia - although non-motor features, including anosmia, constipation, depression, and REM sleep behaviour disorder, can develop years before motor deficits. During later stages of the disease, additional non-motor features, such as autonomic dysfunction, pain, and cognitive decline, can appear (8).

Currently, no cure has been found for Parkinson's disease. However, treatment is available to help relieve symptoms and maintain everyday life. These treatments include:

- supportive therapies, such as physiotherapy
- medication
- surgery (suggested only for some cases)

Since symptoms are usually mild during the preliminary stages of Parkinson's disease, any treatment is not needed. Usually, PD patients need regular appointments with a specialist to monitor their condition since, as with any progressive neurodegenerative disease, symptoms arise with time. As a result of clinical trials, the treatment of Parkinson's disease has made considerable progress, in which new treatments and treatment combinations are compared to standard treatments.

In the past few years, the COVID19 pandemic has exposed the fragility of regional care systems dedicated to chronic neurological diseases such as Parkinson's disease, but, at the same time, it has enhanced the opportunities offered by technological solutions and indicated in telemedicine an essential element of the clinical and rehabilitative management of these conditions. The scientific literature proposes various analysis, monitoring, and training systems for specific sports activities. However, these lack effective integration, so the remote monitoring system is usually independent of the sports activity delivery system and vice versa.

The medical department of the Università Politecnica Delle Marche, in partnership with the Revolt s.r.l. company and the University of Verona, with the project RAPIDO, will develop a high complexity integrated system for telerehabilitation and telemonitoring.

The project is characterized by a) facilitated access (from smartphones, tablets, and PCs) to educational content and videos explaining exercises for motor rehabilitation, selected based on scientific evidence; b) telemonitoring of adherence to rehabilitation protocols and feedback on performance; c) Outcome detection by monitoring health indicators with wearable sensors.

The expected result is the system development to support the rehabilitation management of the PD in distinct stages of the disease, in the long term, reliable, feasible, economically sustainable, and accessible in residential care.

The aim of this experimental dissertation is firstly to describe the technical aspects of the telerehabilitation protocol and the data acquisition infrastructure, then to provide a possible methodology for data analysis to assess the efficacy of the telerehabilitation approach and the effects that the telerehabilitation has on patients' health status and daily living. In detail, a statistical analysis is proposed to quantify the variation of some physiological variables throughout the rehabilitation training. The proposed methodology is applied to the first group of patients enrolled for the pilot study.

1. PARKINSON'S DISEASE (9)

1.1 NEUROPATHOLOGY

PD consists of the degeneration of dopaminergic neurons in the NS and protein aggregates within neurons called Lewy bodies and Lewy neurites (3). It has long been believed that when clinical motor symptoms become apparent, 50-70% of the dopaminergic neurons of the NS have died (10). However, recent studies have shown that, unlike the loss of neurons in the NS, the loss of dopaminergic terminals in the basal ganglia is essential for developing motor symptoms (11).

1.2 EPIDEMIOLOGY

1.2.1. Distribution of the disease

In estimates based on healthcare utilization, the incidence of PD ranges from 5/100,000 to more than 35/100,000 new cases per year (12). From sixty to ninety years, the incidence rate increases 5 to 10 times. The probability of occurrence of PD increases with age. In a meta-analysis of four North American populations, the disease presence increased from less than 1% for 45-year-old men and women to 4% for 54-year-old men and 2% for women 85-and-older (11). Compared with unaffected individuals, the mortality rate will not increase in the first ten years after PD diagnosis but will increase successively (13). With the world's population ageing, the prevalence of PD is expected to increase dramatically, doubling in the next 20 years (14). Consequently, PD's social and economic burden will enhance unless a more effective treatment, cure, or prevention develops (15).

1.2.2. Determinants of disease

Most cases of PD may have a multifactorial aetiology, which is the result of a combination of environmental and genetic factors. Exposure to toxic chemicals and head injuries can increase the risk of appearance of Parkinson's disease, while certain lifestyle factors can reduce the risk. Genetic susceptibility factors can change the impact of environmental exposure. Although identifiable mutations in specific genes cause PD in 5-10% of cases, most patients with PD do not have these mutations. In addition, the most common genetic mutations related to PD have incomplete penetrance, indicating that other genetic or environmental factors are involved. A study comparing the concordance rates of identical twins and fraternal twins estimated heritability rate of PD was only 30%, indicating that most of the risk of PD is related to environmental and behavioural factors (16).

1.2.3. Toxicant chemical exposure

The evidence from studies spanning decades in many populations is that pesticide exposure, agricultural work, or rural living are associated with an increased risk of PD (17). Occupational exposure and passive exposure due to living near pesticide-treated fields are associated with an increased risk of PD. Pesticides related to PD, including paraquat, rotenone, 2,4D, and various dithiocarbonates and organochlorines, can cause experimental Parkinson's syndrome in laboratory studies, supporting these associations to reflect causal effects possibility (17,18). Conversely, good hygiene or healthy eating behaviours can prevent the adverse effects of exposure to pesticides (19,20).

1.2.4. Head Injuries

In most but not all studies, mild to moderate head trauma, occurring decades before the onset of PD, is associated with an increased risk of PD (18,21). The risk increases with the number of head injuries. Genetic predisposition factors, such as mutations in or near the gene encoding α-synuclein, can increase the PD risk by 2 to 5 times.

1.2.5. Lifestyle Factors

Several lifestyle factors are associated with a reduced risk of PD. The most consistent association is cigarette smokers and, in a few studies, tobacco users have a reduced risk of PD (22,23). The higher the duration and frequency of tobacco use, the lower the risk, and there is some evidence of genetic modification. Although a recently completed clinical study failed to detect the disease-relieving effect of nicotine patches in PD patients, nicotine has been thought to play a leading role in this association. The consumption of coffee and caffeine is also associated with a lower risk of PD (24,25), especially among men. This effect is more significant among men with higher coffee consumption and may be more influenced by genetic factors.

Similarly, in some but not all populations, tea drinkers have a reduced risk of PD. On the contrary, a higher dietary intake of dairy products is associated with an increased risk of PD, which may be due to the concentration of toxic substances in milk (26). Other dietary associations generally support a reduced risk of PD for those who eat a healthy diet rich in fruits, vegetables, and grains (27). Physical activity is associated with a lower risk of PD, especially among men, especially when the intensity of physical activity is high, although even moderate levels will reduce the risk (28) (Figure 1). The combined effects of these lifestyle factors seem to be additive, indicating a way to prevent disease (29).

1.3 GENETICS AND PATHOPHYSIOLOGY

Specific genetic factors that play a fundamental role in the risk of PD can be identified in a subset of PD patients (Figure 2). Polymeropoulos et al. discovered a mutation in the NSCA gene for α-synuclein in 1997, which is related to the rare autosomal dominant PD family (30). Families with these hyperpermeable mutations are rare, but this ground-breaking discovery made people realize that even in patients with sporadic PD, α-synuclein is the main component of Lewy bodies. The autosomal dominant PD family, discovered later, has duplication or triple duplication of the α-synuclein gene, which, added to other data, indicates that high α-synuclein levels contribute to the pathogenesis of PD (31).

Mutations in the PARKIN (32) and PINK1 (33) genes cause early-onset autosomal recessive PD. Both PARKIN and PINK1 are related to cellular pathways that involve the preferential degradation of dysfunctional mitochondrial lysosomes through macro-autophagy, a process called "mitochondrial autophagy." Loss of these gene functions leads to impaired mitochondrial autophagy, leading to dysfunctional mitochondria. PARKIN also indirectly regulates the levels of a relevant transcriptional regulator such as PGC1alpha, responsible, in a coordinated manner, for the expression of genes necessary for mitochondrial biogenesis and various antioxidant defences (34). PGC-1alpha levels are low in sporadic PD (35), indicating that these data are unrelated to the rare inherited form of PD. These genetic links to mitochondrial degradation and mitochondrial biogenesis imply dysfunction of mitochondrial turnover in PD.

These genetic data are supplemented by many other data suggesting mitochondrial dysfunction in the pathogenesis of PD. For example, exposure to 1-methyl-4-phenyl 1,2,3,6-tetrahydropyridine (MPTP) toxin can cause the rapid onset of Parkinson's phenotype and the death of dopaminergic neurons in NS might be since mitochondria inhibit complex activities. Rodents' chronic exposure to rotenone is also a potent inhibitor of mitochondrial complex, which can also lead to preferential degeneration of dopaminergic neurons (35), and exposure to pesticides (including rotenone) is a PD risk factor (36).

Mutations in the DJ1 gene can also cause autosomal recessive early-onset PE (37). DJ1 has antioxidant effects through various mechanisms, including regulation of NRF2, a transcription factor that upregulates multiple antioxidant defences and stimulates glutathione synthesis (38).

The mutation in the LRRK2 gene is associated with autosomal dominant PD with incomplete penetrance (the G2019S mutation is about 25%, but the R144G mutation is higher) and is present in about 1% to 2% of all PD patients, and 5% is in familial PD but is higher in specific populations, such as Ashkenazi Jewish descent and North African Berbers (39). Previous studies have shown that LRRK2 mutations lead to increased kinase activity (40) and that LRRK2 kinase inhibitors may be protective (41), although the possibility of kinase loss has been raised (42). Another common genetic factor contributing to the risk of PD is related mutations in the GBA gene associated with autosomal recessive Gaucher disease (43). Carriers of GBA mutations have a 4-fold increased risk of PD, although the risk varies for different GBA mutations. Some studies have shown that PE patients associated with GBA mutations have an increased risk of dementia (44). PD-related GBA mutations can lead to the loss of the activity of the lysosomal enzyme glucocerebrosidase (GCase), and agents that upregulate GCase activity and agents that target "substrate reduction" have shown promise in model animals and are currently undergoing progress in clinical trials (45).

Previously, neuroinflammation was usually seen only as a response to ongoing neurodegeneration. Recent studies have shown that neuroinflammation may be an influential and indispensable factor leading to alpha-nucleoprotein aggregation and neurodegenerative processes (46). Epidemiological studies have provided information on the relationship between disease and peripheral inflammation (for example, type 2 diabetes and inflammatory bowel disease and increased risk of PD (47,48)). Genetic studies have also linked HLA gene variants with the risk of late-onset PD (49).

The genetics of PD is complicated. Common variants can lead to a risk for Parkinson's disease and interact with other genetic and environmental factors. The sizeable genome-wide association study (GWAS) identified 70 sites that affect PD risk (50). Several loci are near genes related to the lysosomal autophagy system and immunity. Both functions are expected to play an essential role in processing misfolded α-synuclein. Acquired (somatic) mitochondrial DNA mutations are increased in NS neurons in early PD and may also play a role (51). Epigenetic factors can also contribute to the pathogenesis of PD (52).

Given the robust genetic and experimental data linking α-synuclein toxicity to PD, many potential neuroprotective strategies focus on the mechanism of removal of α-synuclein aggregates (53,54). Clinical research is currently ongoing, using monoclonal antibody infusion to target oligomeric α-synuclein or a live vaccine strategy. Other strategies use more

indirect methods, such as the ongoing study of nilotinib, a c-Abl inhibitor that can reduce inflammation and promote α-synuclein clearance (55). Other strategies targeting gene-defined subgroups, such as LRRK2 kinase inhibitors or GCase activators, are making progress in clinical trials. Although the current clinical role of genetic testing is limited, it is already a fundamental research tool. Genetic testing will become a routine treatment for all PD patients to guide targeted therapy.

1.4 PATHOANATOMY (56)

1.4.1. Parkinson's disease affects both the motor and limbic systems.

The pathology related to PD is concentrated in the substantia nigra on the surface, and the dopaminergic projection cells rich in neuromelanin are severely lost in the dense part of this nuclear grey. Some subnuclei of the substantia nigra always show extensive changes. However, others were more or less unharmed (10,57–60). Similarly, groups of dopaminergic nerve cells outside the substantia nigra do not tend to have cytoskeletal abnormalities (61,62). There is currently no reasonable explanation for the notorious resistance of these cell populations. The simple description of PD as an isolated disease of the dopaminergic system, on closer examination, proved to be an unacceptable oversimplification of the disease pathology. From the beginning of the disease, damage to the substantia nigra is always accompanied by an impressive extra-substantia nigra pathology. These substantia nigra lesions cause severe damage to the limbic system, the function of the cerebral cortex, and the autonomic regulatory mechanism. Therefore, it is not only the dopaminergic neurons that present pathological changes. In contrast, many other nerve cells showed severe cytoskeletal damage, including glutamatergic, cholinergic, tryptaminergic, GABAergic, noradrenergic, and adrenergic neurons (63–67). Without exception, susceptible nerve cells belong to the group of projection neurons that produce long axons. In contrast, local circuit neurons and short-axon projection cells still do not show changes related to PD.

1.4.2. Organization of the motor system and the limbic system

The human cerebral cortex consists of a broad neocortical area and a small cortical area. All the cortex occupies the anteromedial part of the temporal lobe and contains the higher centre of the limbic system. The motor cortex is divided into the primary area of motor function and the initial processing of information from the sensory organs. Each primary sensory zone is surrounded by unimodal secondary regions, connected to additional unimodal and

heteromodal associated regions (66,68,69). The somatosensory, auditory, and visual stimuli reach multiple related areas of the neocortex through the primary and secondary areas.
Data is transferred to the prefrontal cortex, which is very widespread in humans. The short path leads from this more thoughtful instance in the human brain to the subordinate domain and finally through the pre-motor area to the primary motor domain. However, most information is transmitted through the striatum and cerebellar ring integrated into this pathway. Therefore, most of the basal ganglia, many nuclear greys in the lower brainstem, and the cerebellum are involved in the cortical production regulation (Figure 3a). The neocortex is often overwhelmed by many irrelevant external stimuli and information. Essential data is filtered out of this stream, and only this data passes through many intermediate neocortical relay stations to get to the edge loop gateway. Therefore, information from the neocortex is the principal source of information for the human limbic system. The entorhinal zone and the outer nucleus of the amygdala are the entry points for this highly processed data. The rim ring sends its major efferent nerves from its centre in the direction of the neocortex in the prefrontal area (70–73). Therefore, those impact this crucial part of the neocortex that is also part of the motor system (Figure 3a). The three loops can be identified in Figure 3b. The marginal ring, striatal ring, and cerebellar ring can be identified from left to right. The broad yellow arrow helps to identify them. The schematic diagrams of these systems help to understand the close connection and close relationship between the limbic system on the one hand and the movement system on the other (74–76). The three centres constitute the superior structure of the limbic system: the entorhinal zone and the hippocampal structure, both of which belong to the same cortex and the adjacent subcortical amygdala. These three centres are intricately related to each other. The limbic cycle plays an indispensable role in maintaining emotional balance, learning ability, and memory function. At the same time, it affects sports activities. The limbic system's influence on the prefrontal cortex explains why sports activities reflect an emotional state. Surprisingly, the marginal ring component has undergone significant pathological changes in PD.

1.4.3. PD related alterations to the motor and limbic systems

In PD patients, all three high-level centres of the marginal annulus are affected, and many cortical areas and the subcortical nucleus are severely damaged (Figure 3b). The α-synuclein immune response shows very severe pain in the entorhinal area. Many Lewy neurites extend

to the superficial layer of the cortex, while the deep layer is made up of projection neurons that carry Lewy bodies. This level of damage can completely disrupt the exchange of relevant data between the neocortex and the advanced centre of the limbic system and hinder its influence on the prefrontal cortex. This injury paves the way for mental decline (67,77). For example, damage to the entorhinal area is much more severe than damage to the anterior cingulate cortex. The anterior cingulate gyrus is a typical site of cortical involvement in PD. With the naked eye in immunostained sections, Lesions are usually formed in the hippocampus. A dense network of Lewy neurites forms in the second part of Ammon's horn (78,79). This pathological cortical network continuously evolves in the course of the disease. It is very typical, so only by its appearance can a case be established for the neuropathological diagnosis of Parkinson's disease (66). Severe deterioration of the amygdala is essential to understand the damage associated with the disease (65). For example, areas where the primary efferent nerves go to the ventral striatum, the ventral globe pallidus, the medial thalamus, and the prefrontal cortex, such as the basal nucleus of the amygdala, show many Lewy bodies in their projection neurons. The central amygdalar nucleus has severe cytoskeletal damage, showing many Lewy axons and Lewy bodies of different diameters. Many are linear or discrete droplet-like shapes and require α-synuclein immunostaining for more visible detection (80). The amygdalar central nucleus and the nucleus of the bed at the stria terminals usually have an essential effect on the autonomic and neurosecretory nuclei of the hypothalamus, thus obtaining orientation in most areas of the endocrine system (Figures 3a and b). The severe pathology found in the central amygdala must be detrimental to these functions.

In addition to these tasks, the central nucleus of the amygdala also serves as an orientation centre for processing visceral sensory data and controlling all visceral motor areas of the brainstem and spinal cord. All limbic systems and autonomic nerve centres that are bidirectionally connected to the amygdala show substantial PD-specific damage (63,66,89–91,81–88).

These structures are the grey matter at the periaqueductal, the parabrachial area, the giant cellular nucleus of the reticular structure, the intermediate reticular area, and the dorsal area of the vagus nerve, as well as the regulatory centre of the digestive tract, respiratory organs, and cardiovascular system.

Finally, the central nucleus of the amygdala has a significant effect on all non-thalamic nuclei, with diffuse connection projections to the cerebral cortex and many other structures of the central nervous system. Severe pathological changes related to PD also occur in these diffuse projection nuclei, namely the large cholinergic nucleus of the basal forebrain, the nodular papillary GABAergic nucleus of the hypothalamus, the serotonergic raphe nucleus, and the ventral non-dopaminergic nucleus of the electron energy nucleus. The rampant destruction of the central nucleus of the amygdala and the nucleus with diffuse protrusions dramatically reduces the overall entrance to the cerebral cortex.

1.5 PARKINSON'S TREATMENTS

Physiotherapists can use manipulations and exercises to relieve muscle stiffness and joint pain. Physical therapists aim to promote movement and improve gait and flexibility. They also try to improve the health of patients and their ability to manage things on their own.

1.5.1. Occupational therapy

Occupational therapists can identify difficult areas in daily life, such as getting dressed or going to a local store. They can help patients develop practical solutions and ensure that the home is safe and meticulously organized. Those therapies will help maintain independence for as long as possible.

1.5.2. Speech and language therapy

Many people with Parkinson's disease have dysphagia and speech problems. Speech and language therapists can often help improve these problems by teaching oral and swallowing exercises or providing assistive technology.

1.5.3. Diet advice

For some people with Parkinson's disease, changing their eating habits can help improve specific symptoms. These changes may include:

- The increase of fibre in the diet and fluids reduces constipation and avoids undesirable weight loss.
- The increased amount of salt in the diet and eating smaller meals to avoid low blood pressure problems, such as dizziness when standing up quickly

1.5.4. Medication

Drugs could be administered to improve the main symptoms of PD, such as tremors and movement problems. The problem is that not all available drugs are helpful for everyone;

moreover, each drug's short-term and long-term effects are different. There are three commonly used drugs:

- Levodopa
- Dopamine agonist
- Monoamine-oxidase B inhibitor

The variable and often unpredictable complications seen in clinical response to L-dopa are experienced by 80% of chronically treated PD patients. Disabling and distressing LID represents a fundamental therapeutic issue in the later stages of PD, occurring in most patients after 5-10 years of treatment. Reduction of L-dopa dosage may improve them but always with a concomitant defection in anti-parkinsonian efficacy. Balancing this trade-off becomes a significant challenge for the management of advanced PD.

Motor fluctuation refers to alternating *on* and *off* periods in patients with PD. After L-dopa administration, improvement in parkinsonian symptoms is described as *on*, whereas a return of parkinsonian symptoms is termed *off*. The response to L-dopa is divided into three-time frames according to dopamine levels:

- The *dose begin*s when the patient first notices an improvement in symptoms and switches on.
- The *peak dose*: or *maximal improvement in parkinsonian symptoms*.
- The *end of dose*: when parkinsonian symptoms re-emerge. For the proper diagnosis and management of motor fluctuations, a detailed history of the patient's symptoms related to the L-dopa timing is critical (92).

Levodopa-Induced Dyskinesia (LID): Patients develop involuntary movements associated with motor fluctuations, also known as dyskinesias. The term dyskinesia collectively groups all the disorders that cause hyperkinetic movements or combinations. This movement could be different: for instance, *chorea* consists of unwanted, rapid movements characterized by random and erratic amplitude with high inter-and intra-individual variability; *myoclonus* indicates involuntary movements that are more rapid and briefer than chorea; *athetosis* (also called slow chorea) relates to slow, continuous, writhing movements involving the distal segments of limbs. Athetosis is considered phenomenologically to lie between dystonia and chorea in the hyperkinetic movement spectrum. On the other end, the *ballism* applies to large amplitude and rapid (ballistic) involuntary movements in the proximal limb muscles (93).

Some critical clinical issues help manage dyskinesia in PD:

- The phenomenology of the movements, whether chorea, dystonia, ballism, and body distribution (legs versus upper body).
- The timing of dyskinesia concerning the level of L-dopa: *high dose*, implying dyskinesia seen at the peak dose, or *low dose*, when dopamine levels are reduced or absent, at the onset and end of L-dopa dose or in the off-periods (also known as diphasic dyskinesias and primarily off-period dystonia).
- Whether the patient is aware of the movements, many patients do not recognize LID or may not experience any disability from the movements. It should be highlighted that treating every dyskinesia is not necessarily essential; instead, one should prevent worsening or reduce only disabling, bothersome dyskinesia with medical or surgical strategies (92).

Dyskinesias are most common at the peak level of L-dopa action (*peak-dose dyskinesia*); such LID can be a mixture of chorea, ballism, dystonia, and, to a lesser extent, myoclonus. It affects limbs, the head, and the trunk. Rarer forms of LID can affect the eyes and respiratory muscles (92). In their mildest form, dyskinesia may not bother the patient, who may prefer mobility associated with it to immobility with no dyskinesia. With the worsening of dyskinesia, significant limitations ensue. LID leads to exhaustion and fatigue, always with concomitant weight loss. The risk of injury and fall is constant for the patient and carers. The painful dystonia causes pronounced discomfort and physical limitation. The patients often limit their social life leading to isolation, frustration, anger, and depression. Rare fatalities (related to cardiac arrhythmias) have also been reported. From the view of health care services, dyskinesias have the worst consequences. LID tends to appear when the disease is advancing, and it is often needed to increase the dose of levodopa. A dose increase is associated with dyskinesia worsening, while a dose reduction leads to poor control of Parkinson's disease. LID is associated with poor quality of life and increased healthcare costs (94).

1.5.5. Surgery

Most patients with PD are treated with drugs, although sometimes deep brain stimulation is used. This surgical intervention can be performed in specialized neuroscience centres, but it is not suitable for everyone.

Deep brain stimulation involves the surgical implantation of a pulse generator like a pacemaker into the chest wall. The generator relates to 1 or 2 thin wires placed under the skin and precisely inserted into specific brain areas. The pulse generator generates a small electrical current that passes through the wire and stimulates the part of the brain affected by PD. Although surgery cannot cure the disease, it can relieve symptoms in some people.

1.5.6. Treating additional symptoms

In addition to the main symptoms of movement problems, patients may also experience collateral symptoms that may require specific treatments. These symptoms include:

- *Depression and anxiety*: can be treated with self-care measures such as Exercise, psychotherapy, or medications.
- *Sleep problems (insomnia*): can be improved by changing the bedtime routine.
- *Erectile dysfunction*: treated with medications.
- *Excessive sweating (hyperhidrosis):* prescription antiperspirants or surgery may be used in severe cases to reduce this condition.
- *Dysphagia (dysphagia)* can be improved by eating softened food or using a feeding tube in more severe cases.
- *Excessive drooling* can be improved with swallowing exercises, surgery, or medication in severe cases.
- *Urinary incontinence*: In severe cases, the pelvic floor muscles can be strengthened with exercise, medication, or surgery.
- *Dementia*: in some cases, can be used cognitive therapy or medication.

1.5.7. Complementary and alternative therapies

Some people with Parkinson's disease will seek complementary therapies to help them feel better. Many complementary therapies and therapies claim to alleviate the symptoms of PD. Nevertheless, there is no clinical evidence that they can effectively control the symptoms. Most people believe that add-on treatment does not have harmful effects. However, some may be harmful and should not be used in medication prescribed by a doctor. Certain herbs, such as St. John's Wort, may help patients' health if taken with certain drugs used to treat PD.

1.6 LIVING WITH PARKINSON'S DISEASE

1.6.1. Exercise and healthy eating

Regular Exercise relieves muscle stiffness, improves mood, and relieves stress. Patients can perform many activities to stay in shape, from more active sports such as tennis and cycling to less strenuous activities such as walking, gardening, and yoga.

In addition, a balanced diet that includes all food groups can provide the body with the nutrients it needs to stay healthy.

1.6.2. Vaccinations

All people are encouraged with long-term illnesses to get the flu vaccine every autumn. It is also generally recommended pneumococcal vaccine, a one-time injection, prevents serious chest infections called pneumococcal pneumonia.

1.6.3. Interpersonal Relationships

Being diagnosed with a long-term illness like PD puts the patient, family, and friends under pressure. It can be challenging to talk about the illness with other people, even if they are close. Facing worsening symptoms, such as increased difficulty exercising, can make the patient feel depressed and frustrated. The spouse, partner, or caregiver also inevitably feels anxious or depressed. Express feelings candidly and let family and friends know what they could do, helping to make the situation better.

1.6.4. Support

For any questions about the patient's condition, the general practitioner or PD nurse can help. It is also helpful to talk to a trained counsellor, psychologist, or someone from a professional helpline. It is helpful for some people to talk to other Parkinson's patients in local support groups or Internet chat rooms.

1.6.5. Care and support services

It is worth taking the time to consider specific needs and what can help to achieve the best quality of life. For example, it is essential to consider equipment, help at home, and home renovations.

1.6.6. Complex Parkinson's disease and palliative care

The complex Parkinson's disease is the stage where the symptoms cannot be controlled consistently by treatment, or the patient has uncontrollable twitching movements (disabling

dyskinesia). Symptoms can be alleviated under the supervision of doctors specifically interested in Parkinson's disease by adjusting or adding some drugs for PD treatment.

As PD progresses, patients will be invited to discuss the palliative care they want with the medical team near the end of their lives. When the disease cannot be cured anymore, palliative care tries to reduce symptoms. However, it also aims to make the person as comfortable as possible at the end of life by alleviating pain and other distressing symptoms while providing psychological, social, and spiritual support to patients and families. In a hospice or at home, foster family, or hospital, palliative care can be provided.

2. TELEMONITORING AND TELERIABILITATION

Neurodegenerative diseases (NDDs) currently affect more than thirty million people worldwide and are a diverse group of debilitating and incurable diseases with devastating consequences for patients and their families. NDD is characterized by progressive degeneration of central nervous system structure and function due to an unknown cause of idiopathic mechanisms or, rarely, hereditary disorders. NDD includes a large number of patients, including both common and rare diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) (95). The most obvious risk factor for developing this condition is ageing, and the prevalence of NDD increases significantly as the average age of the population increases (96) (97). This direct and indirect increase puts a heavy burden on the healthcare system and the economy (98–101).

As the illness progresses, NDD is characterized by a continuous decline in motor and/or cognitive function, making the journey to the clinic stressful and difficult for patients and caregivers. In addition, lack of adequate transportation, being in rural areas, and limited financial resources can exacerbate the problem. As a result, patient-physician contact becomes very difficult in care, monitoring, and intervention. (102).

Therefore, telemedicine and telehealth approaches can be valuable to address this challenge, especially in this scenario. Telemedicine, by definition, is the dissemination of health-related services using electronic technology, which can improve the continuity of care for patients with chronic NDD. (103). Telehealth has several facets (104):

- **Telehealth**: a generic term for technical health information services, health education, and health services.
- **Telemedicine**: refers to distance education of medical services via telecommunications. Telemedicine refers to providing remote clinical services to patients using information technology and electronic communications (video consultation, medical image evaluation, etc.).
- **Telecoaching**: Coaching is provided via electronic media. In healthcare, this means the process of care and patient management through device use.
- **Telecare**: monitor sensitive patients with alarms, sensors, and other devices to help people lead longer and more independent lives. Telecare consists of assistive technologies and services tailored to individual needs. Monitor activity changes.

Despite the theoretical possibility of applying a telemedicine approach in some domains, the use of this service is still limited. However, when the recent COVID 19 pandemic acted, medical services for chronic illnesses were suddenly interrupted. In fact, except for visits with urgent functions, outpatient follow-up visits have been immediately interrupted, which inevitably creates feelings of loss and abandonment concerning the lack of tailored medical and psychological assistance. For these reasons, switching to alternative forms of care, including telemedicine and telehealth, is essential to prevent a more significant loss of function.

2.1 A REVIEW OF TELEMEDICINE IN PARKINSON'S DISEASE

Almost all Parkinson's disease symptoms measurements are performed clinically, not reflecting everyday situations. The most widely used rating scale for PD symptoms is the Unified Parkinson's Disease Rating Scale (MDS UPDRS), consisting of interviews asking patients for historical information regarding the previous week's mention and a clinical rating scale. Clinical features include semi-quantitative functional (disordered) motor skills (105). UPDRS is not optimal for several reasons: first, UPDRS assessments are based on subjective reports by patients and semi-objective observations by clinicians. This lack of objectivity allows for variation and potential biases in diagnoses or determinations of PD-related motor states. Second, UPDRS assessments only capture the short, discrete periods that patients spend in the clinic with their physician. These NSapshots do not necessarily reflect the more variable, day-to-day state of the patient's PD symptoms in an environment outside of the clinic. As Parkinson's disease progresses to more advanced stages, severe motor and cognitive impairment can occur. Some patients may not travel long distances, like walking distances, like regular follow-up visits at tertiary medical centres. However, the scientific consensus is that new evaluation strategies, especially those with high ecological validity, multiple evaluation times, and effective effectiveness, are needed (106). Telemedicine comprehends the remote delivery of health care services.

Quantitative evaluation using wearable devices can provide continuous, objective, and environmentally sound data collection. It can be applied frequently at short intervals outside the clinic to track symptom changes in real-time. This approach can also improve patient-physician interactions, influence treatment decisions, and improve patients' overall health.

These metrics can also be used as outcome measures in clinical trials, allowing frequent evaluation (e.g., at home). This wearable probe is of particular interest because it can be worn discreetly and therefore does not significantly affect the person who wears the probe during testing or in everyday life. It can also measure movement and be attached to almost any body part that may exhibit symptoms of interest (106).

The first study using these sensors was conducted ten years ago and focused on evaluating tremors and dyskinesia. By bypassing the information received from these sensors back to individual users, they can learn more about each sign of disease and how to respond to symptoms associated with disease, which can provide additional motivation to users. Telemedicine must reliably assess motor function for existing treatment models improvement, and these outcomes can be achieved using various devices. Ferreira et al.'s study (107) used a SENSEPARK system, an objective system capable of quantitative and continuous monitoring of 22 PD patients using wearable sensors.

Other applications have been examined in locomotor oscillation: one study (108) validated clinically an algorithm capable of detecting and quantifying leg dyskinesia using a single ankle-worn sensor. The ability to efficiently capture motor features of PD could be useful in identifying potential candidates for advanced therapies. For example, Heldman et al. (109) found that baseline rates for advanced therapies were significantly higher for patients with reported telemonitoring. compared with standard care alone (63.6% vs 11.8%, p-value <0.01). However, immediate concern about the validity of remote physical examination is also raised since stiffness and balance cannot be assessed remotely.

In addition, other parts of the neurological exam, such as reflexes or eye movements, are more difficult to assess. The first telehealth studies focused primarily on this topic: Samii and colleagues (110) reported the use of telemedicine for more than three years to provide follow-up care. For thirty-four patients with PD, all the Parkinson's Disease Rating Scale (UPDRS) measures were demonstrated using improved video quality. The reliability of a modified UPDRS that removes stiffness and recoil factors compared with a standard motor scale was also confirmed in a secondary analysis of the CALM-PD study (111). In addition, when travel and accommodation costs are considered, significant resource savings can be achieved (110). Cubo et al. validated the cost-effectiveness of home mobility monitoring plus standard visits versus office visits alone in 35 PD patients (112): an effective home care

model cost in terms of functional status, motor impairment, and motor complications, as assessed by UPDRS II, III, and IV.

Concerning the integrated care model, some studies have also evaluated the economic benefits of telemedicine. For example, Dorsey et al. (113) have examined this approach's feasibility, effectiveness, and economic benefits. The author conducted a randomized controlled trial of twenty patients, eleven individual visits, and nine telemedicine specialists. Each visit to telemedicine saves participants an average of one hundred miles of travel and has relevant financial value. However, there was no difference in the quality of life between the two groups (p-value = 0.61). It results in a similar quality of life in a one-year randomized controlled trial conducted by Beck et al. (114): In the 195 cohorts, the standard treatments are complemented by four virtual visits by video conference. Patients were compared. Telemedicine groups have consistently had financial benefits but did not improve the quality of life of those who received virtual home visits.

Darner et al. (115) provided a group of 50 Parkinson's patients with a live-stream telemedicine home-care service 24 hours a day, seven days a week. One year later, from the beginning, they found that Parkinson's Disease Questionnaire 39 (PDQ39) scores improved significantly, but not the UPDRS-, MMSE, or Hoehn & Yahr (H&Y) scores.

As part of an integrated care system, one of the earliest telemedicine applications was related to fragile and advanced PD patients. Biglan et al. (116) used live teleconference technology to provide care to a patient residing in a remote nursing home over eight months, which improved motor and cognitive symptoms and satisfaction from the patient's perspective.

In a randomized controlled trial (24), the possibility of providing care via telemedicine was considered for patients residing in nursing homes(117): the participants were randomized to receive telemedicine care or their usual care, and three telemedicine visits were performed over six months. Patients receiving telemedicine completed almost all scheduled visits and showed significant improvement in their quality of life and motor performance. Moreover, cognitive impairment is highly likely to occur when considering the remote evaluation of advanced-stage PD patients. It may represent one of the most relevant nonmotor features: a pilot study from Abdolahi and colleagues (111) tested whether, in 17 individuals with

movement disorders, the MoCA examinations could be remotely assessed via web-based video conferencing, confirming the feasibility of this approach.

One of the first telemedicine applications as part of an integrative care model involving patients with mild and advanced PD is found in the Biglan et al. (23) study. They used telemedicine to provide care to a patient residing in a remote nursing home for eight months, resulting in improvements in motor and cognitive symptoms and patient satisfaction. The feasibility of providing telehealth care to patients in nursing homes was also considered in a randomized controlled trial (24): participants were randomized to receive telemedicine or their usual care, and three telemedicine visits were made in six months. Patients treated with telemedicine performed all their scheduled visits and showed significant improvements in quality of life and mobility. In addition, when telemedicine is considered for patients with advanced CNS disorders, cognitive impairment is also highly likely; this may represent a feature unrelated to movement. An experimental study by Abdolahi and colleagues (18) examined whether MoCA tests can be evaluated remotely via online video conferencing in seventeen people with movement disorders, confirming the feasibility of this approach.

If telemedicine is a treasured aid for sufferers who can not carry out routine observe-up visits due to lengthy tour distances or widespread motor and nonmotor deterioration, the control of intermediate PD ranges must be addressed. Marzinzik and colleagues (118) analyzed information from seventy-eight sufferers worried in an incorporated care program (ICP). Patients submitted home videos to the treatment team via the Internet, and an average of 3.2 videos were posted per day during the 30-day evaluation period. After termination of ICP, UPDRS scores were significantly lower than baseline, and the information in the questionnaire demonstrated the general acceptability and practicality of this method. Another advantage of using ICP is that it can better communicate the dynamics of motor vibrations with a consistent recording schedule.

Although many benefits can be observed, the implementation and use of telemedicine programs have raised concerns about the doctor-patient relationship. Several studies evaluated patient perception. Qiang JK and Marras (119) distributed satisfaction questionnaires to 34 and 103 non-telemedicine users. 29/34 users were interested in continuing to use telemedicine, and non-users (55/103) were interested in using telemedicine as a partial or complete replacement for in-person visits. The authors found that lower H&Y

levels and longer travel times were the most important predictors of interest in telemedicine. The interest in telemedicine use was also assessed in a national randomized controlled trial conducted by Dorsey and colleagues in 2016 (120): 11.734 individuals visited the study's website, and 927 individuals submitted electronic interest forms; this is clear indication of the high interest in receiving remote care. Another study (121) confirmed the increased interest of patients in telemedicine: the main advantages included access to specialists (62%), convenience (60%), and time savings (59%). Therefore, these studies suggest that telemedicine does not affect the doctor-patient relationship.

Other exciting developments in telemedicine include speech and physical rehabilitation. Howell et al. (122) showed that using Lee Silverman voice therapy (LSVT) combined with a webcam in three PD patients yielded similar benefits compared to facial treatment. Comparable results have been found in other studies in subjects receiving remote therapy rather than conventional individual LSVT.
(122,123). Moreover, language assessments can be reliably conducted online. Constantinescu and co-workers (124) assessed the level of agreement between an online assessment of hypomotor dysarthria in 61 patients and a face-to-face assessment by two speech pathologists. There were no significant parametric differences between the two approaches in most cases.

Regarding telerehabilitation, a randomized controlled trial (125) compared, in 76 patients, the treatment with virtual reality (VR) rehabilitation and in-clinic sensory integration balance training (SIBT) and found that, in the VR group, there was a significant improvement in the Berg Balance Scale. Another trial (126) compares 20 subjects that have been randomized to obtain both telecoach-assisted exercising (TAE) and self-regulated exercising (SRE). Both groups acquired the equal eight-week exercising prescription with mixed energy and cardio exercise. The authors observed that the TAE individuals executed a greater sturdy attendance (99.2%) than SRE individuals. Moreover, many nonmotor symptoms may benefit from telemedicine, such as depression and anxiety. A randomized controlled trial (127) proved the feasibility of telephone-administered Cognitive Behavioral Therapy (CBT) to tackle these nonmotor features. Another recent trial (128) further confirmed these results: 72 PD patients were randomized to telephone-based cognitive-behavioural treatment (T-CBT) or treatment as usual. The Hamilton Depression Rating Scale score improved significantly in

T-CBT, with a persistent benefit over a six-month follow-up (p-value < 0.01). Another study (129) investigated the feasibility and patient satisfaction of telepsychiatric services in 33 PD patients who received 19 telepsychiatric sessions and 62 personal visits. Some technical aspects required further optimization, but patients were generally satisfied.

Another relevant PD management issue is related to advanced therapies: a study performed by Willows and colleagues (130) evaluated levodopa-carbidopa intestinal gel (LCIG) home titration in 14 patients via telemedicine. The median time required for dosage adjustment was lower than hospital titration, with both patients' and health practitioners' satisfaction. Additionally, when considering Deep Brain Stimulation (DBS), telehealth resources have been proved beneficial: the experience of the Ontario Telemedicine Network (131) confirmed in 141 patients retrospectively analyzed the feasibility of telemedicine, which provided adequate interventions allowing, at the same time, a significant reduction in the burden and costs of travelling. Another study (132) in six patients has investigated the feasibility of a technical system incorporating a kinematic sensor capable of detecting motor symptoms. Real-time remote control of an apomorphine pump: this approach was allowed for three patients and could be adjusted more easily.

3. CLINICAL STUDY

The experimental study, named RAPIDO “teleRiabilitazione per i mAlati di Parkinson In qualsiasi staDiO,” involves patients affected by Parkinson's disease at any stage in a telerehabilitation process that lasts for three months.

The study was performed in the Neurorehabilitation Clinic, Department of Experimental and Clinical Medicine, Marche Polytechnic University, and at the Department of Neuroscience, Biomedicine, and Movement of the University of Verona within the Integrated University Hospital (AOUI) of Verona. The selection of participants depends on different criteria.

***Inclusion criteria*:**

- Each subject needs to be at least 18 years old (either male or female).
- Parkinson's disease needs to be diagnosed according to Movement Disorders Society criteria (Postuma RB et al., Movement disorders 2015).
- Everyone needs to give his written, informed consent.

Exclusion criteria:

- Moderate-to-severe cognitive impairment (MoCA≤18) or other known factors interfering with the ability to interact with the platform (e.g., poor visual acuity, lack of family support).
- Comorbidities impact survival and autonomy or contraindicate the performance of physical exercise (e.g., neoplastic severe, cardiovascular diseases that are not pharmacologically controlled, including hypertension or arterial hypotension, cardiac arrhythmias, heart failure, musculoskeletal diseases, vertiginous syndrome).
- Depression or other severe neuropsychiatric disorders.
- Change in drug therapy regimen for less than four weeks.

Subjects deemed eligible based on the inclusion/exclusion criteria will be allowed to carry out a learning session on the telerehabilitation and telemonitoring system in the laboratory during the screening visit aimed at the enrolment validation in the study.

Those who confirm their interest in the system at the end of the trial session:

- They will receive a smartwatch for three months and be instructed to wear it 24 hours a day, for at least five days/week, and always during the exercise program.
- They will receive, for three months, a tablet programmed with their user credentials to access the telerehabilitation platform. They will be instructed to carry out sessions lasting

(even if not continuous) 45 minutes/day, at least three times/week (for no less than 27 sessions in total, equal to 1200 minutes of training), including a personalized exercise program about the functional profile.

The exercises will be exemplified by videos, accessible on the online platform, specially developed by clinical researchers and oriented to train skills belonging to four different domains: postural alignment skills (Domain 1), strategies for overcoming freezing and preventing falls (Domain 2), ability to articulate speech (Domain 3), compensatory postures for swallowing (Domain 4). The exercises of each domain will be proposed in levels of increasing complexity and based on the risk of falling evaluated with the item postural instability of the UPDRS part III to allow a better personalization of the training experience and promote motivation to the regularity of the Exercise. Regularly (every 15 + 3 days), they will receive a video call on the tablet from the clinical reference centre to verify the correct use of the devices and the level of adherence to the exercise program, as well as to agree on the adaptation of the training program to the progression of the user's skills.

***Primary Endpoints**:* Feasibility of the system, measured through the following indicators:

- Feasibility of use: measured by the ratio between the number of sessions attended and the minimum number of sessions planned (expected value: >75%); duration of training carried out/total duration of training planned. Expected value: >75%.
- Security of the system: adverse events that occurred during the use of the telerehabilitation system and that may or may not be related to the treatment. Expected value: 0.
- System usability measured by: SYSTEM USABILITY SCALE (SUS)

Secondary Endpoints:

- User satisfaction: rated using the Global Rating of Change for each patient – PGRC (Likert scale). Expected value: >50% delighted users.
- Compliance with the monitoring system: duration of smartwatch activation made/minimum expected activation duration. Expected value: > 75%.
- The clinical centre’s feasibility of assessments carried out remotely: several online assessments/minimum numbers of evaluations envisaged. Expected value: >75%.
- Progression of the disease (in terms of motor and non-motor disorders, limitation of autonomy, and complications of drug therapy), evaluated by UPDRS (Part I, II, III, and

IV) and NMSS; expected value: < 5% worsening of the scores detected in the individual scales of measurement at 3 and 6 months, compared to baseline

- Quality of life: evaluated by PDQ8 and EuroQol 5D; Expected value: >10% improvement in scores at 3 and 6 months from baseline
- Care load perceived by the caregiver: assessed through Zarit burden interview; expected: < 5% worsening of scores at 3 and 6 months from baseline
- Care needs: assessed through Client Service Receipt Inventory; Expected value: < 5% change in scores at 3 and 6 months from baseline.

During the trial, there are three evaluation sessions at the clinical centre of reference: at enrollment, after the signing of informed consent and screening visit (T0), and at the end of the 12 weeks of use of the telemonitoring and telerehabilitation system (T3m), and follow-up at six months (T6m) from the baseline visit.

The study will be submitted for approbation to the Regional Ethics Committee (CERM). Any adverse events (EAs) reported by the patient or detected by healthcare professionals will be recorded and reported to CERM, as required by local regulations. The study will be conducted in full compliance with the current revision of the Declaration of Helsinki. The study is designed to ensure adherence to the principles of Good Clinical Practice (GCP) and compliance with Italian law. Subjects will be asked to give and sign informed consent to the study. Any changes to the protocol will require the approval of the CERM before the implementation of such changes. The investigator will present, store, and archive the essential documents of the study according to GCP. The investigator will keep a list of identification codes of all enrolled subjects separate from the data collection system. Instead, it will be stored in a computer platform where only an alphanumeric code will identify all the participants. The investigator will be personally responsible for the data protection for seven years. The data results will be published in international journals and discussed at scientific congresses, and the identity of the subjects will always be kept anonymous.

At least one hundred subjects (50 subjects in each Clinical Center) will be enrolled. Considering a dropout quota of less than 20%, the sample available for evaluating the outcome will be eighty subjects. The sample size was calculated using the confidence interval method (95% CI), the exact Clopper-Pearson method, and a 95% confidence level. A sample size of eighty subjects for each group allows for evaluating feasibility (estimated

as a percentage of completed sessions) of at least 75%, with a range amplitude of 19.95% (95% CI 64.06-84.01).

3. 1. TECHNICAL ASPECTS

For the delivery of the devices, each patient went to the "Ospedale Riuniti" in Ancona, where he was first subjected to the examination of the medical team and then had an interview with the technical team. The technical team consists of Lucia Pepa, researcher, Antonio Sabatelli, and Antonia Antoniello, PhD students.

The team has developed an app that obtains the raw acceleration data and all the infrastructure that allows the exchange of patient data: from the Garmin server, under prior authorization from the subject, through HTTP calls, the data are sent to the dedicated server of the project. In addition, to allow the rehabilitation at the patient's home, the team has created an online platform that the patient can access with their confidential credentials and in which he will find the rehabilitation protocol assigned.

The telemonitoring and telerehabilitation system comprises two main subsystems: a local edge/fog computing system and a remote system that exposes RESTful services. The local system is composed of a smartwatch with integrated sensors to monitor physiological variables and an edge/fog computing node to receive smartwatch data via Bluetooth and communicate with the remote system. The remote system is a server application (hosted by the Italian company Aruba Spa) that follows the Software-As-A-Service paradigm and accomplishes the following functions: storage of monitoring data received by the edge/fog node via HTTP protocol; exposure of web services to manage (deliver and keep track) rehabilitation therapies, accessible through a dedicated client web application at the URL https://www.rehab-univpm.it/public/#/home.

Each patient received detailed instructions on using the devices provided to complete the trial successfully. The first group of five patients was enlisted to test the entire infrastructure and received:

- A ***Samsung A7 tablet*** act as the edge/fog computing node of the local subsystem, and that can be used to navigate the web application with rehabilitation therapies. The tablet is already configured with the user account for each patient and in which the dedicated mobile app to communicate with the smartwatch. To avoid difficulties of use, even for

less experienced users, a quick link to the web application site where the subject finds its rehabilitation protocol was created in the Google Chrome app.

- A ***Garmin Vivosmart 4*** smartwatch is a slim, smart fitness tracker that blends fashionable design with stylish metal accents and a bright, easy-to-read display. Advanced sleep monitoring includes REM sleep, fitness, and health monitoring tools, including wrist-based heart rate, all-day stress tracking, relaxation breathing timer, VO2 max, Body Battery™ energy monitor, etc. Dedicated activity timers for walks, runs, strength training, yoga, pool swims, and others; connects to your compatible smartphone's GPS for accurate tracking during outdoor walks and runs.

The smartwatch requires an initial setup through ***Garmin Connect™*** (Figure 5), a mobile or web tool for tracking, analyzing, and sharing health and fitness activities recorded by the Garmin device. It is a user-friendly application where digital insights give helpful hints tailored to the user. Garmin Connect™ is packed with useful features: view today's health data in vivid detail on the personalized My Day page; analyze activities and their related statistics, and review personal records for steps, distance, and pace.

All data recorded are stored on the Garmin servers and then sent to the remote server through an HTTP POST request. Thus, collected data can be onload and analyzed according to the purposes of the study.

Subjects were instructed to wear the smartwatch continuously, seven days a week, 24 hours a day, for the three months they were undergoing rehabilitation therapy. The patient did not do any exercise for one week to record the pre-therapy baseline values. One week after the delivery of the devices, he/she began the rehabilitation therapy by doing the predefined exercises that he/she found on the web platform.

In detail, the patient login with his/her credentials in the web application to access the reserved area, which shows the rehabilitation therapy assigned by the clinician and the progress (in terms of percentage of completion) reached by the patient (Figure 5. a). The patient can easily start a new training session of the rehabilitation protocol through a user-friendly interface that automatically presents the next scheduled training session and guides the patient throughout that training session's exercises (Figure 5. b). When the patient completes the last exercise programmed for a training session, the web application notifies the successful end of the training session with a message on the screen (Figure 5. c).

A dedicated database hosted in the remote server of the system stores all relevant data about telerehabilitation: rehabilitation protocols programmed by clinicians for each specific patient and training sessions performed by patients (start and end time).

4. DATA ANALYSIS

4. 1. DATA ACQUIRED

For each patient, all the data recorded by the Garmin device are stored in the Garmin server and then, through some HTTP calls, are sent to the remote server implemented for the project.

This section details the data available for each summary type. Summary records are the core data transfer method in the Garmin Health API, and each summary corresponds to a different ping notification type. The maximum query range for all summary data endpoints is 24 hours after upload time. The upload time corresponds to the time the user synchronized the data, not the timestamp of the summary data itself.

The summary data obtained via push notifications follow the same data model described in this section.

4.1.1. Daily Summaries

Daily summaries offer a high-level view of the user's entire day. They correspond to the data found on the "My Day" section of Garmin Connect. Daily summaries are the most used and are often the foundation of a Health API integration. A successful response is a JSON array containing zero to many daily summaries.

Each daily summary may contain the field found in Table 1 in the Tables section.

Example:


```
[
    {
        "summaryId": "EXAMPLE_67891",
        "calendarDate": "2016-01-11",
        "activityType": "WALKING,"
        "activeKilocalories": 321,
        "bmrKilocalories": 1731,
        "consumedCalories": 1121,
        "steps": 4210,
        "distanceInMeters": 3146.5,
        "durationInSeconds": 86400,
        "activeTimeInSeconds": 12240,
```

```
        “startTimeInSeconds”: 1452470400,
        “startTimeOffsetInSeconds”: 3600,
        “moderateIntensityDurationInSeconds”: 81870,
        “vigorousIntensityDurationInSeconds”: 4530,
        “floorsClimbed”: 8,
        “minHeartRateInBeatsPerMinute”: 59,
        “averageHeartRateInBeatsPerMinute”: 64,
        “maxHeartRateInBeatsPerMinute”: 112,
        “timeOffsetHeartRateSamples”: {
                “15”: 75”30”: 75,
                “3180”: 76,
                “3195”: 65,
                “3210”: 65,
                “3225”: 73,
                “3240”: 74,
                “3255”: 74
        },
        “averageStressLevel”: 43,
        “maxStressLevel”: 87,
        “stressDurationInSeconds”: 13620,
        “restStressDurationInSeconds”: 7600,
        “activityStressDurationInSeconds”: 3450,
        “lowStressDurationInSeconds”: 6700,
        “mediumStressDurationInSeconds”: 4350,
        “highStressDurationInSeconds”: 108000,
        “stressQualifier”: “stressful_awake,”
        “stepsGoal”: 4500,
        “netKilocaloriesGoal”: 2010,
        “intensityDurationGoalInSeconds”: 1500,
        “floorsClimbedGoal”: 18 16
    }
]
```

4.1.2. Epoch Summaries

This service provides the ability to retrieve a list of summaries containing wellness data for a specific time range. Epoch summary records contain much of the same data available in Daily summaries but with 15-minute time-slice granularity.

There is one record for each activity type monitored within an individual epoch. For example, if the user were sedentary for five minutes, walked for five minutes, and then ran for five minutes for 15 minutes, three activity records would be generated for that single 15-minute epoch. The duration value would be 900 seconds for all three records, but the active time for each would be 300 seconds.

A duration of fewer than 900 seconds indicates that the user synced data during the middle of an epoch. That epoch record will be replaced with a 900-second-duration epoch covering the entire span on the user's next sync. As such, and to accommodate users with multiple devices, it is important that new epochs always replace existing epochs with the same startTimeInSeconds. The most recent update from the Health API will always reflect the most recent data in Garmin Connect.

Epoch data is useful when attempting to construct charts showing intraday wellness data. An example of this in Garmin Connect is the Steps Details chart that graphs step count changes throughout the user’s day.

Each wellness monitoring summary may contain the field found in Table 2 in the Tables section.

Example:


```
[
    {
        “summaryId”: “EXAMPLE_1234”,
        “activityType”: “SEDENTARY,”
        “activeKilocalories”: 0,
        “steps”: 0,
        “distanceInMeters”: 0.0,
        “durationInSeconds”: 900,
        “activeTimeInSeconds”: 600,
        “met”: 1.0,
        “intensity”: “SEDENTARY,”
```

```
        “startTimeInSeconds”: 1454418900,
        “startTimeOffsetInSeconds”: 3600
    },
    {
        “summaryId”: “EXAMPLE_5678”,
        “activityType”: “RUNNING,”
        “activeKilocalories”: 257,
        “steps”: 427,
        “distanceInMeters”: 222.07,
        “durationInSeconds”: 900,
        “activeTimeInSeconds”: 300,
        “met”: 9.894117,
        “intensity”: “HIGHLY_ACTIVE,”
        “startTimeInSeconds”: 1454418900,
        “startTimeOffsetInSeconds”: 3600
    }
]
```


4.1.3. Stress Details Summaries

Stress Details summaries contain the user's stress level values for a given day. Stress levels are provided as 3-minute averages of the real-time stress scores generated on the device, with values ranging from 1 to 100. A value of -1 means there was insufficient data to detect stress, and -2 means there was too much motion (e.g., the user was walking or running). Scores between 1 and 25 are considered "rest" (i.e., not stressful), 26-50 as "low" stress, 51-75 "medium" stress, and 76-100 as "high" stress. These numbers are derived based on a combination of many device sensors. They will automatically adjust to the device's wearer and gain accuracy over time as the stress algorithms learn the user's natural biometric norms. Stress values from the Health API are exactly the stress values shown on Garmin Connect. A successful response is a JSON array containing zero to numerous stress details summaries. Each stress details summary may contain the field found in Table 3 in the Tables section.

Example:


```
[
    {
```

```
        "summaryId": "EXAMPLE_6789124",
        "calendarDate": "2017-03-23",
        "startTimeInSeconds": 1490245200,
        "startTimeOffsetInSeconds": 0,
        "durationInSeconds": 540,
        "timeOffsetStressLevelValues": {
                "0": 18,
                "180": 51,
                "360": 28,
                "540": 29
                },
        "timeOffsetBodyBatteryDetails": {
                "0": 55,
                "180": 56,
                "360": 59
        }
}
]
```


4.1.4. Sleep Summaries

Sleep summaries are data records representing how long the user slept and the automatically classified sleep levels during that sleep event (e.g., light, deep periods) based on data generated by the user's device. Users may generate sleep data in three diverse ways. Some older Garmin devices (e.g., first-generation vívofit) allow users to manually place the device in sleep mode. Newer devices do not have this option and instead auto-detect sleep if it occurs between the user's Bed/Waketime range configured in Garmin Connect. Users may also self-report sleep information using Garmin Connect. Sleep records from the Health API are labelled to identify how the sleep data were generated. This allows partners to accept/reject various methods of collecting Sleep data. Recommended usage for this field is to filter out validation types that are not desired rather than accept only certain validation types to prevent lost data in the future if new validation types are added, as, by default, Garmin Connect displays records of all types.

Unlike Daily summaries associated with a given day on a midnight-to-midnight basis, Sleep summaries are associated with a user's overnight sleep range. Most will start on one calendar day and end on the next calendar day. However, two different Sleep summaries can begin on the same day if, for example, the user goes to bed after midnight, wakes up, and then goes to bed prior to midnight the next evening. Sleep levels from the Health API correspond to the sleep levels graph found in Garmin Connect. In Garmin Connect and the Health API, the sleep summary will include REM sleep if the user's device is capable of REM sleep analysis. Users without REM-capable devices or REM-capable devices that have not been updated to REM-capable firmware are limited to only deep, light, and awake sleep levels. REM sleep will only be generated if the REM-capable device is set as the preferred activity tracker and worn during sleep.

Some pulse-oximetry-enabled devices will generate SpO2 values during sleep for use in sleep analysis. They are included in the sleep summary for reference if such values are generated.

Sleep score enabled devices will generate sleep scores for sleep analysis if the user has the device set as the primary active tracker in the user's Garmin Connect account. If your application utilizes sleep scores, please ensure any qualitative values are represented using the same descriptors provided through the API to avoid misleading or confusing End Users as described in the API License Agreement. A successful response is a JSON array containing zero to many sleep summaries.

Each sleep summary may contain the field found in Table 4 in the table section.

Example:


```
[
    {
        “summaryId”: “EXAMPLE_567890”,
        “calendarDate”: “2016-01-10”,
        “durationInSeconds”: 15264,
        “startTimeInSeconds”: 1452419581,
        “startTimeOffsetInSeconds”: 7200,
        “unmeasurableSleepDurationInSeconds”: 0,
        “deepSleepDurationInSeconds”: 11231,
        “lightSleepDurationInSeconds”: 3541,
```

```
        “remSleepInSeconds”: 0,
        “awakeDurationInSeconds”: 492,
        “sleepLevelsMap”: {
                “deep”: [
                        {
                                “startTimeInSeconds”: 1452419581,
                                “endTimeInSeconds”: 1452478724
                        }
                ],
                “light”: [
                        {
                                “startTimeInSeconds”: 1452478725,
                                “endTimeInSeconds”: 1452479725
                        }, {
                                “startTimeInSeconds”: 1452481725,
                                “endTimeInSeconds”: 1452484266
                        }
                ]
        },
        “validation”: “DEVICE”
},
{
        “summaryId”: “EXAMPLE_567891”,
        “durationInSeconds”: 11900,
        “startTimeInSeconds”: 1452467493,
        “startTimeOffsetInSeconds”: 7200,
        “unmeasurableSleepDurationInSeconds”: 0,
        “deepSleepDurationInSeconds”: 9446,
        “lightSleepDurationInSeconds”: 0,
        “remSleepInSeconds”: 2142,
        “awakeDurationInSeconds”: 312,
        “sleepLevelsMap”: {
```

```
        “deep”: [
                {
                        “startTimeInSeconds”: 1452467493,
                        “endTimeInSeconds”: 1452476939
                },
        “light”: [
                {
                        “startTimeInSeconds”: 1452478725,
                        “endTimeInSeconds”: 1452479725
                }, {
                        “startTimeInSeconds”: 1452481725,
                        “endTimeInSeconds”: 1452484266
                }
        ],
        “rem”: [
                {
                        “startTimeInSeconds”: 1452476940,
                        “endTimeInSeconds”: 1452479082
                }
        ]
},
“validation”: “DEVICE,” “timeOffsetSleepRespiration”: {
        “60”: 15.31,
        “120”: 14.58,
        “180”: 12.73,
        “240”: 12.87
},
“timeOffsetSleepSpo2”: {
        “0”: 95,
        “60”: 96,
        “120”: 97,
        “180”: 93,
```

```
                "240": 94,
                "300": 95,
                "360": 96
            },
            "overallSleepScore": {
                "value": 87,
                "qualifierKey": "GOOD"
                },
            "sleepScores": {
                "totalDuration": {
                    "qualifierKey": "EXCELLENT"
                },
                "stress": {
                    "qualifierKey": "EXCELLENT"
                },
                "awakeCount": {
                    "qualifierKey": "FAIR"
                },
                "remPercentage": {
                    "qualifierKey": "FAIR"
                },
                "restlesNSess": {
                    "qualifierKey": "GOOD"
                },
                "lightPercentage": {
                    "qualifierKey": "GOOD"
                },
                "deepPercentage": {
                    "qualifierKey": "POOR"
                }
            }
    },
```

```
    {
        "summaryId": "x-EXAMPLE",
        "calendarDate": "2021-01-29",
        "durationInSeconds": 28260,
        "startTimeInSeconds": 1611840660,
        "startTimeOffsetInSeconds": 32400,
        "unmeasurableSleepInSeconds": 0,
        "deepSleepDurationInSeconds": 0,
        "lightSleepDurationInSeconds": 0,
        "remSleepInSeconds": 0,
        "awakeDurationInSeconds": 0,
        "validation": "OFF_WRIST",
        "timeOffsetSleepSpo2": {},
        "timeOffsetSleepRespiration": {}
    }
]
```


4. 2. DATA PROCESSING

The data collected by the smartwatch for each of the five patients were analyzed. The data of the first week of acquisition let to know the pre-training values of each subject. The patients start their training protocol in the second week, so it will be useful to analyze how the data vary over time with the exercise sessions performed.

Each patient has their folder on the server, and the data collected daily is stored in special folders. Data were processed offline after acquisition using the Python 3.10 programming language. The reason that drove the choice is that Python is an interpreted, object-oriented, high-level programming language with dynamic semantics. Its high-level built-in data structures, combined with dynamic typing and dynamic binding, make it extremely appealing for Rapid Application Development and scripting or glue language for connecting existing components. Python's concise, easy-to-learn syntax promotes readability, which lowers software maintenance costs. Python facilitates program flexibility and code reuse by supporting modules and packages. The Python interpreter and its substantial standard library are free to download and distribute in source or binary form for all major platforms.

This section will describe all the processes that led to the results. It is necessary to underline that it is an ongoing project, now into its initial stage, so all the steps and results could be affected by this condition and by the reduced amount of data.

All scripts were designed so that they could be automated as much as possible and analyze the data without the constant changes by the programmer. The only manual changes required are increasing the range of days that the program uses to load the data into the LoadJson.py file is the possible addition of UsedIDs as new patients are enrolled.

4.2.1. DataFrame creation

All folders containing the different JSON files for each patient were downloaded locally. In this phase, two functions have been created: the first one allows loading the JSON files and normalizing semi-structured JSON data into a flat table. This action was necessary because of the presence of grafted JSONs that caused the impossibility of the conversion into a table directly during the loading phase; the second one creates for each patient a DataFrame in which each row corresponds to the daily acquisition, and each column represents an entry of the JSON file. For each of the five patients, four DataFrames were created, one for dailies summaries, one for stress summaries, one for sleep summaries, and one for epochs summaries.

4.2.2. DataFrames preliminary and visual analysis

Different approaches were used for each of the DataFrames in relation to the data contained. In all cases, a function was created that would first allow for basic statistical analysis to see the maximum, minimum, mean, standard deviation, and 25, 50 75 percentile values of each column. A k-th percentile (percentile score or centile) is a score below which a given percentage k of scores in a frequency distribution falls (exclusive definition) or a score at or below which a given percentage falls (inclusive definition) (inclusive definition). The 50th percentile (median) is, for example, the score below which (exclusively) or at or below which (inclusively) 50% of the scores in the distribution can be found.

However, in this case, the interesting thing is the count entry that shows the sum of the values in the column. Observing the total sum of days allows you to understand how many days the subject has worn the watch compared to the amount of time passed since delivery. Another procedure carried out on all DataFrames was converting the index column in

DateTime format to be used in the appropriate libraries and to make the time analysis more functional.

Dailies DataFrame: there are information for calendarDate, steps, distanceInMeters, activeTimeInSeconds, activeKilocalories, consumedCalories, moderateIntensityDurationInSeconds, vigorousIntensityDurationInSeconds, floorsClimbed, minHeartRateInBeatsPerMinute, averageHeartRateInBeatsPerMinute, maxHeartRateInBeatsPerMinute, restingHeartRateInBeatsPerMinute, averageStressLevel, maxStressLevel, stressDurationInSeconds, restStressDurationInSeconds, activityStressDurationInSeconds, lowStressDurationInSeconds, mediumStressDurationInSeconds, highStressDurationInSeconds, stressQualifier e *timeOffsetHeartRateSamples* recorded with a 15-second frequency throughout the day resulting in a total of 4896 columns. These were replaced by their standard deviation calculated for each row and inserted as a new column in the DataFrame. A first visual analysis was performed by plotting the individual variables over time: numerical values were plotted as lines. The x-axis value corresponds to the acquisition day and the y-axis value to the recorded value. Null values, i.e., those where the recording was missing, were lacking in the line plot. The values recorded as strings, and in this case, the *stressQualifier*s, are plotted as a bar graph representing the frequency of acquisition of the given value throughout the patient's monitoring period.

Sleep DataFrame provides details on calendarDate, startTimeInSeconds, durationInSeconds, unmeasurableSleepInSeconds, deepSleepDurationInSeconds, lightSleepDurationInSeconds, remSleepInSeconds, awakeDurationInSeconds, Validation, sleepLevelsMap.deep, sleepLevelsMap.light, sleepLevelsMap.rem, sleepLevelsMap.awake. The four columns concerning the sleepLevelMap are loaded as JSONs reporting the time in seconds at the beginning and end of each recorded episode. Considering the presence of the total duration in seconds of the rem phase of deep and light sleep and of the phase in which the subject was awake, the number of recorded episodes was extracted from the sleep maps. Four columns were created for each variable to replace the related column. Also, in this case, the numerical values were plotted as lines where on the x-axis there is the day and, on the y-axis, the recorded value, while for the validation column, a bar graph was created to show the frequency of the recorded value over time.

Stress DataFrame contains information regarding calendarDate, startTimeInSeconds, durationInSeconds, timeOffsetStressLevelValues and timeOffseBodyBatteryValues recorded every 180 seconds for a total of 480 columns. Each row of the last two variables was analyzed to extract the maximum, minimum, mean, median, standard deviation, and 25, 50, and 75 percentile and then replace the original columns. The numerical data thus obtained were plotted as lines whose coordinates were the day and the acquisition value.

Epochs DataFrame contains information recorded every 15 minutes, and the columns' *activityType* and *intensity* were analyzed. For both variables, considering every day, the number of times the given activity/intensity was recorded was calculated. The data obtained were plotted in a bar graph that reported the sum of the single values obtained for each day.

4.2.3. DataFrame statistical analysis – One way ANOVA

The one-way analysis of variance (ANOVA) determines if the means of three or more independent (unrelated) groups differ statistically. In our case, the distinct groups represent the different weeks of the rehabilitation process. The one-way ANOVA compares the means between the groups under examination and determines whether those means are statistically significantly different from each other (p-value < 0.05). Specifically, it tests the null hypothesis:

$$H_0: \mu_1 = \mu_2 = \mu_3 = \cdots = \mu_k$$

where μ = group mean and k = number of groups. If, however, the one-way ANOVA returns a statistically significant result, it is accepted the alternative hypothesis (HA), which is that at least two group means are statistically significantly different from each other.

The one-way ANOVA is an omnibus test statistic and cannot demonstrate which groups were statistically significantly different from each other. It means that only at least two groups were. A post hoc test is used to determine which groups differ. Since those tests are performed to confirm where the differences occurred between groups, they should only be run when it is shown an overall statistically significant difference in group means (i.e., a statistically significant one-way ANOVA result). Post hoc tests are termed a posteriori tests; they are performed after the event (the event, in this case, being a study). There are many different post hoc tests: with the assumption to handle groups of the same size, in this work,

it is used Tukey's honestly significant difference (HSD) post hoc test accounts for multiple comparisons and corrects for family-wise error rate (FWER).

To compare the means and variability of each variable during weeks, box plots are displayed. Those plots are also helpful in understanding the results of Tukey's test.

ANOVA test has some assumptions:

- The ***dependent variable is normally distributed*** in each group being compared in the one-way ANOVA (technically, it is the residuals that need to be normally distributed, but the results will be the same). The model's residuals are extracted and then plotted into a **Quantile-Quantile** plot: When the quantiles of two variables are plotted against each other. This plot summarizes whether the distributions of two variables are similar or not with respect to the locations. A quantitative result is then extracted through the **Shapiro-Wilk test**. The normality assumption is only needed for small sample sizes (N ≤ 20 or so). For larger sample sizes, the sampling distribution of the mean is always normal, regardless of how values are distributed in the population. This phenomenon is known as the central limit theorem. And the consequence is that many test results are unaffected by even severe violations of normality. So, if sample sizes are reasonable, normality tests are often pointless.
- ***Homogeneity of variances*** means that the population variances in each group are equal. It is **used Levene's Test for Homogeneity of Variances**. It is convenient to know if they have equal mean scores to compare two or more groups on a quantitative variable. This assumption can be safely ignored if all groups, which are compared, has roughly equal sample size. However, if there are sharply different sample sizes, data need to meet the homogeneity assumption. Levene's test requires two assumptions: independent observations and the test variable is quantitative - that is, not nominal or ordinal; both the assumptions are satisfied in the data population.

RESULTS

In this section will be found all results obtained after data analysis.

In the Table 5 is reported the rehabilitation program completion rate and training time for each patient. Then respectively for each patient are reported dailies summaries plots, stress summaries plot, sleep summaries plot and epocs plot. Plot obtained by ***dailies summaries*** data will be plotted in figures 6, 16, 26, 36 respectively for each patient. Plot obtained by ***stress summaries*** data will be plotted in figures 7, 17, 27, 37 respectively for each patient. Plots obtained by ***sleep summaries*** data will be plotted in figures 8, 18, 28, 38 respectively for each patient. Bar plots of ***activity type e intensity*** are shown in figures 9, 19, 29, 39 respectively for each patient.

The results of the ANOVA analysis are reported at the same order for each participant. First it is found the table where there is the outcome of Shapiro-Wilk's test and Leneve's test, values under the level of significance (<0,05) are written in bold type while the name of the variable is written in italics. Then there is the One-way ANOVA resultant p-value. In this case, if the value is under the level of significance (<0,05), both the number and the name of the variable are written in bold. Variables that did not meet the assumptions of the ANOVA remained written in italics. At the end, if Tukey's test is performed, the results are shown. ***Shapiro-Wilk's test*** results and ***Leneve's test*** results are shown in tables: 6, 14, 22, 31 for dailies summary data; 9, 17, 25, 34 for sleep summary data; 11, 19, 28, 36 for stress summary data. ***Quantile-quantile plots*** are shown in figures 10, 20, 30, 40 for dailies summary data; figures 12, 22, 32, 42 for sleep summary data; figures 14, 24, 34, 44 for stress summary data. ***One way ANOVA test*** results are shown in tables 7, 15, 23, 32 for dailies summary data; 10, 18, 26, 35 for sleep summary data; 12, 20, 29, 37 for stress summary data.

Tukey's test results are found in the tables 8, 16, 24, 33 for dailies summary data; 27 for sleep summary data (it is performed only for the third participant); 13, 21, 30, 38 For stress summary data. ***Box plots*** are in the figures 11, 21, 31, 41 for dailies summary data; 13, 23, 33, 43 for sleep summary data; 15, 25, 35, 45 for stress summary data.

DISCUSSION

This section will discuss the data obtained five weeks after the first patient has been enrolled. The results of the ANOVA test will be investigated separately for each patient to see what changes there have been over time in the variables recorded. It is noteworthy to point out again that there are only five subjects enrolled for the first step and at the time of writing this thesis they are between the fourth and fifth week of enrollment. The data collected are too few to make clinical evaluations of the subjects or to assert the actual functionality of the rehabilitation process, but they are enough to design a system of statistical analysis that can evaluate the trend of the parameters, both offline, after downloading the data locally and online in a future practical application. As the number of recorded data increases, it is likely that the data discussed below will vary, but it is assumed that the trend will remain constant. Since patients are enrolled with a week of difference, the analysis for two patients is carried out in five weeks, for the other three patients, the analysis is made in four weeks (in both cases starting from the day in which devices have been delivered).

Firstly, for each subject all recorded variables are plotted against the recording day, when an array of values is recorded for each day, the mean value over the day is considered. Graphs are grouped among the summary they come from: there's one figure with all the figures of dailies variables, one with all the plots of stress variables, one with sleep variables and one figure with bar charts of the activity type and intensity. All these images are needed to show the evolution per day of the parameter of the subject and, they are useful to immediately and visually understand when the smartwatch recorded a null value or if there's a day that the patient did not wear the smartwatch. Due to a technical issue, a few data belonging to the epochs summary are lost: are missing 13/04 for three subjects, and 12/04 for one subject.

In the second instance, are reported the results of the One-way ANOVA test, after the results of the test ensure that the ANOVA assumptions are met. In the end, there are the boxplots that show the mean value and variability for each dependent variable during weeks.

FIRST PARTICIPANT

The subject wears the smartwatch every day but not all nights: sleep data coming from 11/04 and 13/04 are missing. However, no recording issues occur, there's a valid value for all the

variables. The subject has performed the 25% of his rehabilitation schedule for a total amount of two hours and thirteen minutes (Table 5).

Observing the dailies plot (Figure 6) it can be noticed that there's a bit day by day variability in all the variables recorded; only the duration of moderate and vigorous intensity is always zero. This variability is found also in the stress plot (Figure 7) but some small changes could be observed in the stress and body battery: the first decreases and the second increases depicting a more healthy subject condition. The patient never sleeps more than seven hours per night (Figure 8), and his habits are characterized by numerous nocturnal awakenings, but a good rem phase. The type of sleep most often recorded is light sleep.

Into the two bar plots for epochs summaries (Figure 9) is shown, respectively, the kind of activity and the intensity recorded every 15 minutes in a day. Data for the 13/04 report the activity between 00:00 and 00:45, this is the reason why it is recorded as sedentary.

For each summary type, is performed a One-way ANOVA.

Dailies From the Shapiro-Wilk test (Table 6) result that the dependent variables *floorsClimbed*, *activeKilocalories, moderateIntensityDurationInSeconds, vigorousIntensityDurationInSeconds, maxHeartRateInBeatsPerMinute, stdGeartRate!5Seconds, restingHeartRateInBeatsPerMinute, averageStressLevel, mediumStressDurationInSeconds lowStressDurationInSeconds, highStressDurationInSeconds* are not normally distributed. These quantitative results are supported by the qualitative result obtained with the Quantile-quantile plot (Figure 10), where it is possible to see that the variable mentioned before are distributed into a small range of values. Since the number of samples is more than twenty Leneve's test is performed (Table 6). From these test results, the homogeneity of variance assumption is satisfied for all the variables.

The results of the One-way ANOVA test (Table 7) display a statistically significant difference between the mean values of weeks for the *activeKilocalories, stdHeartRate15Seconds, maxStressLevel, restStressDurationInSeconds, lowStressDurationInSeconds* recordings. To understand which couple of weeks has the statistically significant difference a pair-wise analysis through Tukey's test is performed (Table 8). A statistically significant difference of means is found between the first and fourth and the first and fifth week of *activeKilocalories*; the third and fourth week of

stdHeartRate15Seconds, the first and fifth week for *averageStressLevel, stressDurationInSeconds* and *restStressDurationInSeconds.*

Tukey test results are supported by box plots (Figure 11). For all the variables where the ANOVA test results non-significative, the interquartile range of each week overlaps; while for the variables that result significative, the boxes of the weeks that show significance in the Tukey test do not overlap. The first and fourth and the first and fifth boxes of *activeKilocalories*, the third and fourth interquartile ranges of *stdHeartRate15Seconds, and* the first and fifth boxes for *averageStressLevel, stressDurationInSeconds* and *restStressDurationInSeconds* do not overlap. Into the *activeKilocalories* boxes, we can see that the mean value for the fourth and fifth week is lower than those in the previous week, this means that the subject activity is decreased in those weeks compared to the previous weeks. The *stdHeartRate15Seconds* represent the variability of the values of heart rate recorded every 15 seconds, the mean value for each group increases for the first three weeks and then decreases. This phenomenon, perhaps, could be related to the lower activity in those weeks. The mean values for *averageStressLevel* and *stressDurationInSeconds* decreases during weeks while *restStressDurationInSeconds* increases.

The subject is less stressed in the last weeks of recording but increases the time in which he resulted stressed even if it was in a rest condition. The lower activity and stress level does not seem consistent with the training data, according to which the subject continues to carry out his rehabilitation sessions.

Sleep From the Shapiro-Wilk test (Table 9), it results that the dependent variables *deepSleepDurationInSeconds, awakeDurationInSeconds, and Awake_sleep_episodes* are not normally distributed and the Quantile-quantile plots (Figure 12), where it is possible to see that the variables are distributed into a small range of value, support these findings. Since the number of samples is more than twenty the Leneve's test (Table 9) is performed and come's out that the assumption of homogeneity of variance is satisfied for all the variables except *Light_sleep_episodes,* which is into the boundary of the significance value.

The results of the One-way ANOVA test (Table 10) display that there is no significant difference in the mean values of the variables during the week, and for this reason, it is possible to say that there were no changes in the subject's sleeping habits.

Stress From the Shapiro-Wilk test (Table 11) and Quantile-quantile plots (Figure 14) result that *min_ timeOffsetstresslevelvalues, median_ timeOffsetstresslevelvalues, perc50_*

timeOffsetstresslevelvalues, perc75_ timeOffsetstresslevelvalues, max_ timeOffsetBodyBatteryValues, min_ timeOffsetBodyBatteryValues, perc75_ timeOffsetBodyBatteryValues do not satisfy the normal distribution condition. While Leneve's test (Table 11) results that all variables found in the stress summary satisfy the ANOVA assumption of homogeneity of variance.

The result of the ANOVA test (Table 12) shows a statistically significant difference between the mean values of weeks for all the dependent variables except *max_timeOffsetStressLevelValues, min_timeOffsetStressLevelValues, perc50_timeOffsetStressLevelValues* and *std_timeOffsetBodyBatteryValues.*

Performing Tukey's test (Table 13), it is possible to observe that in the variable's *median_timeOffsetStressLevelValues, perc50_timeOffsetStressLevelValues* a significant statistical difference is observed between the first and second and the first and fifth weeks: the mean value registered in those week lowers (Figure 15). The *mean_timeOffsetStressLevelValues* results as a false positive, in fact in the post hoc analysis no pairwise investigation results were significant. The statistically significant difference into the mean values of weeks for *min_timeOffsetBodyBatteryValues, median_timeOffsetBodyBatteryValues, mean_timeOffsetBodyBatteryValues, perc25_timeOffsetBodyBatteryValues and perc50_ timeOffsetBodyBatteryValues* is found between the first and fifth and the second and fifth week, in addition has been detected a p-value lower than 0,05 into the pairwise analysis of fourth and fifth week for *mean_timeOffsetBodyBatteryValues.* The mean values computed from the recorded values of each week increase.

From the analysis, it is possible to say that the stress level of the subject does not change very much along the days, but increases the energy, maybe due to a reduction in daily physical activity.

SECOND PARTICIPANT

The subject wears the smartwatch every day but not all nights: sleep data coming from 9/04, 23/04, 24/04 and 27/04 are missing. Moreover, some recording issues occur in the registration of the stress variables on 14/04 and 24/04. He has performed the 8% of his rehabilitation schedule for a total amount of five minutes, only three sessions are completed: one on 20/04, one on 28/04, and one on 05/05 (Table 5). This participant complained of too

short and easy exercises compared to her training level, and as a consequence she fastly got bored. Also, she was complaining about some annoying characteristics of the client application user interface. These reasons may explain the low progress and compliance of the participant with respect to the telerehabilitation program. Both clinical and technical staff are now updating the rehabilitation protocol and the web application in order to satisfy her requests and guarantee a better user experience as well as a personalized rehabilitation program.

Observing the dailies plot (Figure 16) and activity registered into the epochs' summaries (Figure 19), it is possible to observe that he is an active subject, step, activity time and distance in meters are almost the same in all recording periods; the duration of moderate activity and vigorous activity is higher compared to the other subjects. The recorded heart rate values start to increase into the second part of April and into the May recording, and body battery values (Figure 17) follow the same trend. Stress level, which commonly has the opposite behaviour of body battery, starts to decrease at the same time. This seems to mean that the subject decreases his stress level, and this led to an improvement in his body's condition.

Observing sleep variables instead (Figure 18), it is possible to see that the duration in time is quite always the same with a long rem phase (that is commonly affected by Parkinson's disease, many patients have a very short rem phase) and there are few episodes where he wakes up during the night. This is the only subject where epochs' data of 13/04 are recorded.

For each summary type, is performed a One-way ANOVA.

Dailies From the Shapiro-Wilk test (Table 14) result that the dependent variables *floorsClimbed*, *activeKilocalories, moderateIntensityDurationInSeconds, vigorousIntensityDurationInSeconds, averageHeartRateInBeatsPerMinute, maxHeartRateInBeatsPerMinute, stressDurationInSeconds, restStressDurationInSeconds, activityStressDurationInSeconds, mediumStressDurationInSeconds, highStressDurationInSeconds* are not normally distributed. These quantitative results are supported by the qualitative result obtained with the Quantile-quantile plots (Figure 20), where it is possible to see that the variable mentioned before are distributed into a small range of values. Since the number of samples is more than twenty, Leneve's test (Table 14) is performed. From this test results the homogeneity of variance for all the variables.

The results of the One-way ANOVA test (Table 15) display a statistically significant difference between the mean values of weeks for the *steps*, *distanceInMeters, activeTimeInSeconds, restingHeartRateInBeatsPerMinute, averageStressLevel, stressDurationInSeconds, restStressDurationInSeconds, lowStressDurationInSeconds* recordings. To understand which couple of weeks has the statistically significant difference a pair-wise analysis through Tukey's test is performed (Table 16).

A statistically significant difference of means is found between the first and second, and the second and fourth weeks for *steps* and *distanceInMeters* and the second and fourth weeks for *activeTimeInSeconds.* Into the box plot (Figure 21) we can observe an increase in the variables between the first two weeks, and then a decrease. Among all weeks, the mean value of the three variables is the lowest in the fourth week. Then, the activity starts to increase again into the last analysed week. *restingHeartRate* has a significative difference in means between the first and fourth, and the first and fifth weeks: as previously mentioned, the mean values of the recorded data per week are higher in the fourth- and fifth-week respect to the first one. Stress variables have a statistically significant difference between the third and fifth week, in addition, *stressDurationInSeconds* registered a p-value lower than 0,05 also between the first and fifth week. *lowStressDurationInSeconds* difference of means has a statistical meaning for second and fourth, second and fifth, third and fourth, this and fifth, weeks. In all cases, the data appear to support an improvement in the patient's stress condition.

Sleep The Shapiro-Wilk test attests (Table 17) that the dependent variables *durationInSeconds, lightSleepDurationInSeconds, awakeDurationInSeconds, Deep_sleep_episodes, Awake_sleep_episodes* are not normally distributed and the Quantile-quantile plot (Figure 22), where it is possible to see that the variables are distributed into a small range of value, supports these findings. Since the number of samples is more than twenty the Leneve's test (Table 17) is performed and it comes out that the assumption of homogeneity of variance is satisfied for all the variables except *Light_sleep_episodes,* which is into the boundary of the significance value.

The results of the One-way ANOVA (Table 18) test display that there is no significant difference in the mean values of the variables during the week, and for this reason, it is possible to say that there were no changes in the subject's sleeping habits.

Stress From the Shapiro-Wilk test (Table 19) and Quantile-quantile plots (Figure 24) all variables except *max_timeOffsetStressLevelValues* and *std_timeOffsetStressLevelValues* do not satisfy the assumption of the normal distribution, but due to the sample size and the satisfaction of homogeneity assumption (Table 19), the One-way ANOVA test (Table 20) is performed on all the variables. A p-value lower than 0,05 is computed for all variables except *max_timeOffsetStressLevelValues, min_timeOffsetStressLevelValues* and *std_timeOffsetStressLevelValues.* Tukey's test (Table 21) highlighted the most significant difference between the third and fourth and third and fifth week for all variables. Indeed, by observing the interquartile ranges of variables, it can be noticed that the mean values of stress variables seem to increase till the third week, and then it sharply decreases until the fifth week (Figure 25). Mean values of body battery follow the opposite behaviour: a decrease until the third week and then an increase. This finding supports the idea expressed earlier that the patient's state seems to be improved by decreasing the stress level and increasing energy. However, this improvement cannot be correlated to the effect of the telerehabilitation treatment, due to the small number of completed training sessions. Furthermore, the subject was already in good physical condition at the enrollment, as a consequence, there are not any evident changes over time from the data recorded by the smartwatch. More data and more training sessions are needed to find possible effects of rehabilitation training.

THIRD PARTICIPANT

The subject wears the smartwatch every day but not all nights: sleep data coming from 25/04 and 29/04 are missing. However, no recording issues occur, there's a valid value for all the variables. He has performed the 44% of his rehabilitation schedule for a total amount of seven hours and 16 minutes (Table 5).

Observing the dailies plot (Figure 26) it is visible that there's not so much variability even if in the last week of recording it seems that the general activity of the patient is increasing: steps, the activity time in seconds, the duration of moderate-intensity activity reached values that have never reached into the month before. The variables that describe the heart rate at the beginning have a higher variability that is going to decrease at the beginning of May, it is necessary to underly that the two central weeks, where recorded values are higher, coincide with the beginning of the rehabilitation exercises. The same happens in the stress daily

variable and is confirmed in the stress summary plot (Figure 27), the stress level increases into the two-middle week when the subject starts to perform exercises and in the last week starts to slow down. Contra, the body battery pattern is the opposite: decreases into the middle weeks and at the end start to increase. Those values underline that at the first approach with the exercises the subject was stressed, and his body battery goes down, after only a few weeks he started getting accustomed to the rehabilitation session and his values go better.

The sleep variables instead, seem to not follow any pattern (Figure 28): there's always a day-by-day variability, but Parkinson's disease strongly affects the sleep behaviours, so it should be needed more time to see the effect of the rehabilitation program on the patient's sleep habits. Into the two bar plots for epochs summaries (Figure 29) is shown, respectively, the kind of activity and the intensity recorded every 15 minutes in a day. Data for the 13/04 report the activity between 00:00 and 00:45, this is the reason why it is recorded as sedentary. For each summary type, is performed a One-way ANOVA.

Dailies From the Shapiro-Wilk test (Table 22) result that the dependent variables *floorsClimbed*, *moderateIntensityDurationInSeconds, vigorousIntensityDurationInSeconds, maxHeartRateInBeatsPerMinute, mediumStressDurationInSeconds, highStressDurationInSeconds* are not normally distributed. These quantitative results are supported by the qualitative result obtained with the Quantile-quantile plot (Figure 30), where it is possible to see that the variable mentioned before are distributed into a small range of values. Since the number of samples is more than twenty the Leneve's test is performed (Table 22). From this test results the homogeneity of variance for all the variables except *floorsClimbed.* The analysis of this variable stops, while, all the other variables, since satisfying this assumption, are further analyzed.

The results of the One-way ANOVA test display (Table 23) a statistically significant difference between the mean values of weeks for the *minHeartRateInBeatsPerMinute, averageHeartRateInBeatsPerMinute, restingHeartRateInBeatsPerMinute, averageStressLevel, stressDurationInSeconds, restStressDurationInSeconds, mediumStressDurationInSeconds* recordings. To understand which couple of weeks has the statistically significant difference a pair-wise analysis through Tukey's test is performed (Table 24). A statistically significant difference of means is found between the second and third, and the third and fourth weeks for *minHeartRateInBeatsPerMinute*; the first and

second, the first and fourth and the third and fourth weeks for *averageHeartRateInBeatsPerMinute;* the first and second and the second and third weeks for *restingHeartRateInBeatsPerMinute;* the first and third and the third and fourth week for *averageStressLevel;* the first and second weeks for *stressDurationInSeconds;* the first and third and third and fourth for *restStressDurationInSeconds.* From Tukey's test on *mediumStressDurationInSeconds,* it results that no couple of groups have a statistically significant difference between the mean values. This variable didn't satisfy the normal distribution assumption and, although the analysis was allowed to continue, led to false-positive results. The post hoc analysis is thought to fix those situations.

Tukey test results are corroborated by box plots (Figure 31). For all the variables where the ANOVA test results non significative, the interquartile range of each week overlaps; while for the variables, which results significative, the boxes of the weeks that show significance in the Tukey test do not overlap. The second and third, and the third and fourth boxes of *minHeartRateInBeatsPerMinute* do not overlap; the first and second, the first and fourth and the third and fourth interquartile ranges of *averageHeartRateInBeatsPerMinute* do not overlap*,* and neither the first and second and the second and third boxes of *restingHeartRateInBeatsPerMinute.* Moreover, the mean values of those variables show an increase in the third week (when the subject performs the rehabilitation exercises) and then slow down. If the mean value continues to decrease during weeks, this could mean that the subject is adapting the heart rate to the presence of exercise. The first and third and the third and fourth of *averageStressLevel,* the first and second of *stressDurationInSeconds,* the first and third and third and fourth of *restStressDurationInSeconds* interquartile ranges do not overlap. In the *averageStressLevel* and *stressDurationInSeconds,* the mean values are higher into the middle weeks when the subject starts to perform the exercises, then, in the same way as the heart rate decreases, start to lower in the fourth week. Instead, the mean value of the *restStressDurationInSeconds* decreases for the first three weeks, then increases into the fourth. This means that the time when the subject was stressed while it was in a resting condition is higher in the fourth week. The analysis of more weeks and clinical advice could explain this trend.

Sleep From the Shapiro-Wilk test (Table 25), it results that the dependent variables *deepSleepDurationInSeconds, lightSleepDurationInSeconds, awakeDurationInSeconds, Awake_sleep_episodes* are not normally distributed and Quantile-quantile plots (Figure 32),

where it is possible to see that the variables are distributed into a small range of value, support these findings. Since the number of samples is more than twenty, Leneve's test (Table 25) is performed and come's out that the assumption of homogeneity of variance is satisfied for all the variables.

The results of the One-way ANOVA test (Table 26) display a statistically significant difference, on the boundary of the significance level chosen, only between the mean values of weeks for the *light_sleep_episodes.* Through Tukey's test (Table 27) a statistically significant difference in means is found between the first and third week. Analyzing the boxplots (Figure 33), it is possible to see that the interquartile ranges (considering a single dependent variable) in all the variables overlap, except the boxes of the first and third week of the *light_sleep_episodes.* In the third week, the mean values of the number of episodes recorded in the week are lower than the other week, but we can observe a greater number of rem episodes and very high variability of the number of episodes in which the subject was awake. This should mean that this week the subject's sleep was troubled, he completed the rem phase and then woke up often. This test does not underline many changes in the sleep behaviours of the subject as was anticipated by observing the plotting of variables in time.

Stress From the Shapiro-Wilk test (Table 28), Quantile-quantile plots (Figure 34), and Leneve's test (Table 28) result that all variables found in the stress summary satisfy the ANOVA assumptions except the *min_timeOffsetStressLevelValues,* and for this reason, it is not submitted into the One-way ANOVA test. The result of the ANOVA test (Table 29) shows a statistically significant difference between the mean values of weeks for all the dependent variables except *max_timeOffsetStressLevelValues* and *std_timeOffsetBodyBatteryValues.*

Performing Tukey's test (Table 30), it is possible to observe that in the variable's *median_timeOffsetStressLevelValues, mean_timeOffsetStressLevelValues, perc50_timeOffsetStressLevelValues* a significant statistical difference is observed between the first and third weeks, the second and fourth and the third and fourth. In the variables *perc50_timeOffsetStressLevelValues, median_timeOffsetBodyBatteryValues, mean_timeOffsetBodyBatteryValues, perc25_timeOffsetBodyBatteryValues, perc50_timeOffsetBodyBatteryValues* the statistically significant difference is found between the first and third and the third and fourth weeks, while into *std_timeOffsetstresslevelvalues, min_timeOffsetBodyBatteryValues* between the first and

second and the second and third weeks. At the end for *perc25_timeOffsetStressLevelValues, perc75_timeOffsetBodyBatteryValues* Tukey's considered significant only the p-value obtained through the pairwise analysis of the third and fourth week. Whereas the meaning of the stress level and body battery is antithetical, the significance obtained through the test and then observing the mean values of weeks into the box plots (Figure 35) emphasize that the first two weeks of exercise increase the stress level of the subject and decrease his energies, but at the fourth week the situation is reversed: stress level is lower, and body battery is higher. Could the reason be that the subject is getting used to the exercises? More data and a clinical opinion are needed to have an answer to this question.

FOURTH PARTICIPANT

The subject wears the smartwatch every day but not all nights: there are seven days of sleep data missing, for this reason, the ANOVA test on sleep data will be performed on three groups. In addition, some recoding issues occur in the registration of 12 /04 and 12/04 data. The participant has performed the 14% of his rehabilitation schedule for a total amount of one hour and ten minutes (Table 5), only five sessions are completed: one on 22/04, one on 24/04, one on 26/04, and two on 09/05.

Observing the dailies plot (Figure 36), stress plot (Figure 37) and sleep plots (Figure 38), the reordered values have not so much variability. One interesting thing is that the epochs' activity plot (Figure 39) is registered many times a *running* activity, more than in the other participants.

For each summary type, a One-way ANOVA is performed.

Dailies From the Shapiro-Wilk test (Table 31) result that the dependent variables *moderateIntensityDurationInSeconds, vigorousIntensityDurationInSeconds, activityStressDurationInSeconds, highStressDurationInSeconds* are not normally distributed. These quantitative results are validated by examining the residual distribution in the Quantile-quantile plots (Figure 40). Since the number of samples is more than twenty, Leneve's test is performed (Table 31) and homogeneity of variance is ensured for all the variables.

The results of the One-way ANOVA test display (Table 32) a statistically significant difference between the mean values of weeks for the *stressDurationInSeconds and mediumStressDurationInSeconds* recordings. To understand which couple of weeks has the

statistically significant difference a pair-wise analysis through Tukey's test is performed (Table 33).

The pairwise analysis between the weeks of *stressDurationInSeconds* reported no significant difference among the mean values, while a p-value lower than 0,05 is found between the second and fourth week. Into the box plot (Figure 41) it is possible to observe that many interquartile ranges for more than one variable, including *stressDurationInSeconds,* do not overlap, meaning that there's a difference in the mean value and the variability of values recorded in those weeks, but this difference is not enough to reach the significance value chosen. Further investigation and more data could lead to more significative results.

Sleep The Shapiro-Wilk test (Table 34) attests that the dependent variables *deepSleepDurationInSeconds, awakeDurationInSeconds, Deep_sleep_episodes, Awake_sleep_episodes* are not normally distributed and Quantile-quantile plots (Figure 42), where it is possible to see that the variables are distributed into a small range of value, supports these findings. Since the number of samples is more than twenty, Leneve's test (Table 34) is performed, and it comes out that the assumption of homogeneity of variance is satisfied for all the variables.

The results of the One-way ANOVA test (Table 35) display that there is no significant difference in the mean values of the variables during the week, and for this reason, it is possible to say that there were no changes in the subject's sleeping habits.

Stress From the Shapiro-Wilk (Table 36) test and Quantile-quantile plots (Figure 44) *max_timeOffsetStressLevelValues, min_timeOffsetStressLevelValues, std_timeOffsetStressLevelValues, perc25_timeOffsetStressLevelValues, max_timeOffsetBodyBatteryValues, min_timeOffsetBodyBatteryValues* and *perc25_timeOffsetBodyBatteryValues* do not satisfy the assumption of the normal distribution, but due to the sample size and the satisfaction of homogeneity assumption (Table 36), the One-way ANOVA test (Table 37) is performed on all the variables. A p-value lower than 0,05 is computed for all *max_timeOffsetStressLevelValues, std_timeOffsetStressLevelValues, max_timeOffsetBodyBatteryValues,* and *std_ timeOffsetBodyBatteryValues.* Tukey's test (Table 38) highlighted the most significant difference between the first and second, the first and third, the first and fourth weeks both for *max_timeOffsetStressLevelValues* and *max_timeOffsetBodyBatteryValues,* where the mean value increases for both the variables (Figure 45). For

std_timeOffsetStressLevelValues, and *std_ timeOffsetBodyBatteryValues* the statistically significant difference is found between the first and second week, but then, for the stress level the mean value remains quite the same, for the body battery variable the mean values start to decrease denoting lower energy.

FIFTH PARTICIPANT

The participant, upon delivery of the devices, advised the entire team that due to personal reasons he would not be able to begin rehabilitation therapy until May. As of the day that it was decided to conclude data collection for this thesis work, the subject had not yet performed any training sessions. Given the ultimate purpose of the project, which is to evaluate whether telerehabilitation can be functional for the patient's health and considering that the method of data analysis proposed in this thesis work is already exemplified by the other four subjects, I think it is inconsistent to report the results obtained from monitoring the patient's parameters alone. Later, when he will start performing the exercises, the effects of training on the patient can be evaluated statistically.

CONCLUSION

The objective of this experimental thesis was a preliminary evaluation of a telemonitoring and telerehabilitation system for people with Parkinson's disease. Initially, an effort was made to clarify and bring to attention all facets of Parkinson's disease, such as its most important clinical features, by investigating possible causes, analyzing symptoms, and the effects of this pathology on everyday life. Over the years, few systems have been created that would allow telerehabilitation and telemonitoring of patients, who were often subjected to sporadic rehabilitation sessions or clinical evaluations. With the Covid-19 pandemic, it was realized how necessary it is to follow patients remotely as well. Therefore, a telemonitoring and telerehabilitation system was designed, developed and tested in a pilot trial on 5 patients. The system is composed of a smartwatch, to continuously record physiological data and information about the user health status and motor activity, and a remote server hosting the telerehabilitation services, accessible through a client web application. Participants should login their reserved area where they find the rehabilitation program that clinicians customized for his/her personal needs.

The main purpose of this experimental dissertation is to give a possible methodology for data analysis to assess the efficacity of the telerehabilitation approach and the goods that the telerehabilitation has on cases' health status and diurnal living. In detail, a statistical analysis methos is proposed: the One-way ANOVA test is performed on all acquired variables, analyzing how the mean values and standard deviation per week changes. This method helps to understand, both graphically and numerically what is the health parameter evolution in time. Obtained results show that the recorded values move, throughout the rehabilitation session, to a healthier condition.

Even with few data, and few participants, this pilot study gives an idea of different approaches to rehabilitation, one patient completed all the rehabilitation session in the scheduled time, the other participants are a little behind in the rehabilitation program and finally one participant did not conduct any of the sessions. It was seen that the subject that attended the scheduled training sessions, as programmed by clinicians, reached the most important improvements in heath status.

Obtained findings have to be confirmed with the study of a larger sample of patients who have gone through the three months of telerehabilitation, that the proposed study may gain

clinical relevance and that therefore telerehabilitation can be adopted into patients' daily therapies.

This is only the first step in bringing the study closer to application in daily practice, further work is needed. It is intended to try to create a platform that is as interactive as possible, allowing the rehabilitation plan to be modified on the go, also based on patient feedback. An algorithm is to be created that, starting from the raw acceleration data, can evaluate the movements of the upper limbs to give an assessment of movement. It is also desired to show patients the results obtained from the statistical analysis while in the process of telerehabilitation.

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FIGURE

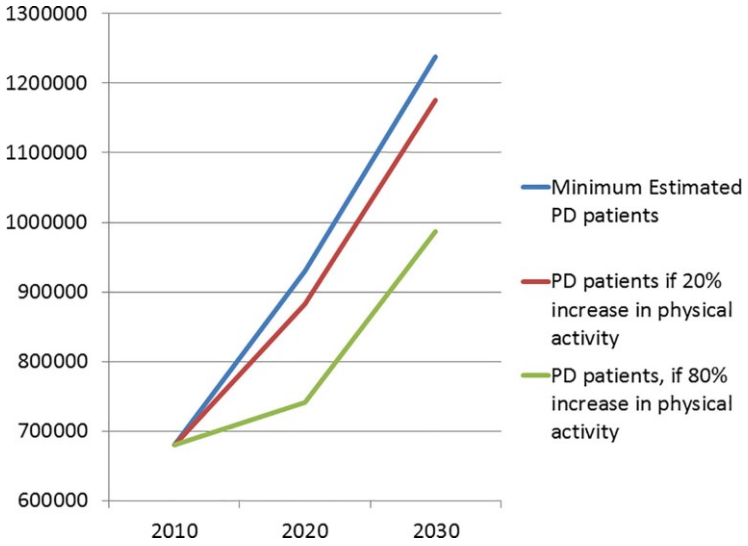


Figure 1. Estimated number of people with PD in the US (blue line) & the projected reduction in PD if physical activity in adults increases by 20% (red line) or 80% (green line). Estimates are based on Marras et.al., 2018 (9).

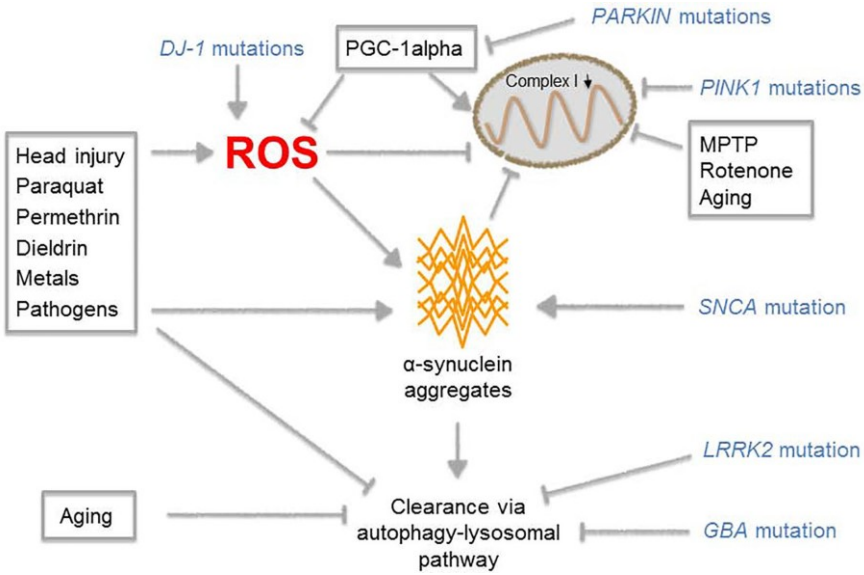


Figure 2. Environmental and genetic factors influence PD pathogenesis by impacting similar pathways, including mitochondrial function, oxidative stress, α-synuclein aggregation, and clearance pathways for abnormal proteins (9).

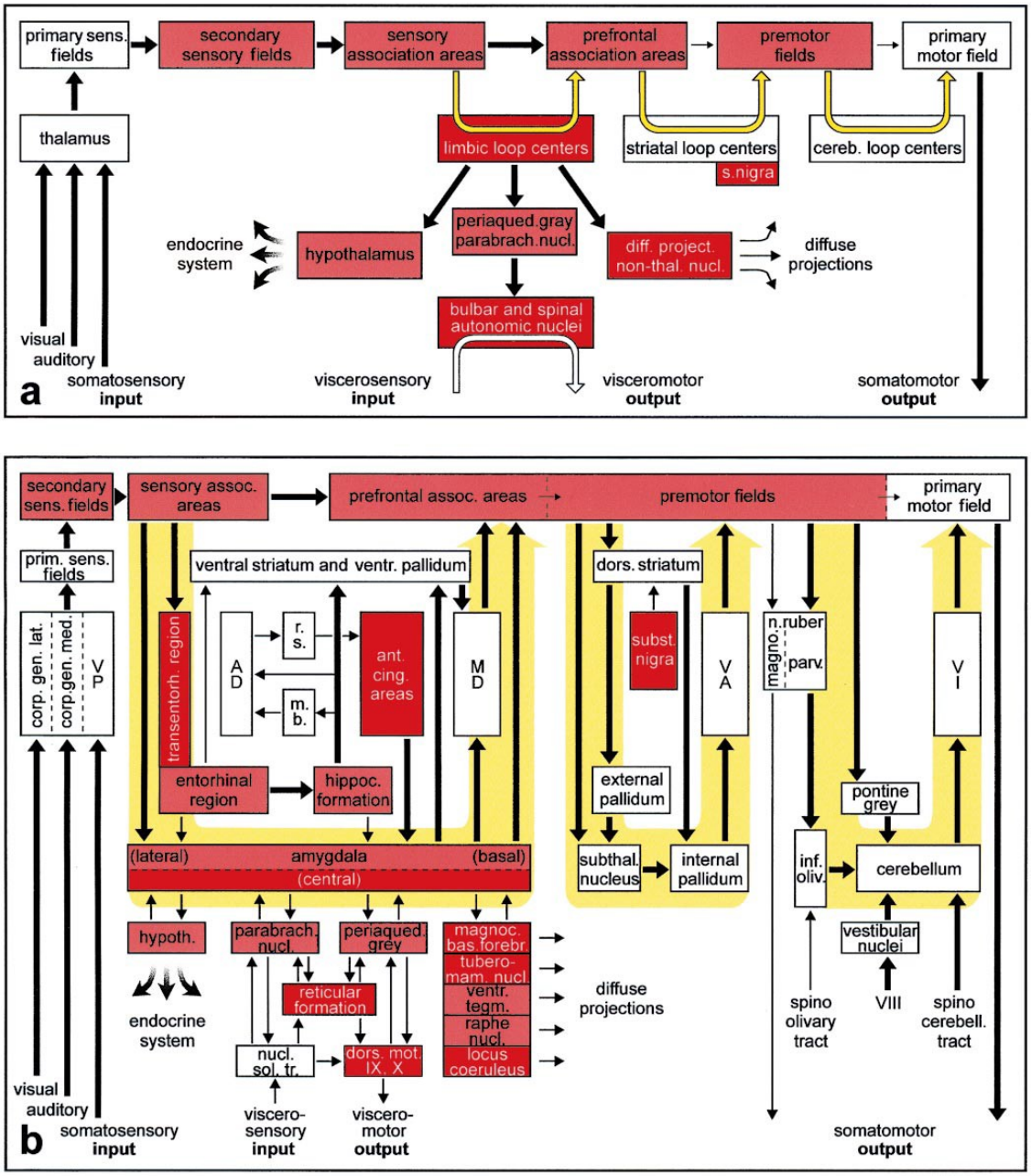


Figure 3. Schematic representation of the limbic system and the motor system. The diagram appears in two forms: the first is highly simplified to recognize the essential connections (**a**), whereas the second is more complex (**b**). The summary diagrams depict the most critical limbic and motor system centres. The damaged regions appear in red to illustrate the extent of the lesions which consistently develop in the brains of patients with Parkinson's disease. Both diagrams show the pathways by which sensory information typically proceeds through neocortical sensory areas and travels via long corticocortical projections to the prefrontal association areas. Short pathways lead away from the prefrontal

cortex to the primary motor field. The striatal and cerebellar loops provide significant routes of transport for this information. Other pathways that convey information from the sensory neocortical association areas meet in the entorhinal region and amygdala, thereby establishing the afferent arm of the limbic loop. Projections from the entorhinal region, the amygdala, and the hippocampal formation contribute to the efferent arm of the limbic loop heading toward the prefrontal cortex. The amygdala integrates exteroceptive sensory data with interoceptive stimuli from autonomic centres. Many descending projections of amygdala subnuclei terminate in nuclei regulating endocrine and autonomic functions. In addition, the amygdala sends efferent connections to all non-thalamic nuclei, which is a non-specific manner project upon the cerebral cortex and other components of the central nervous system. Proceeding from left to right, the limbic loop, striatal loop, and cerebellar loop can be identified, and their recognition is facilitated by the broad yellow arrows. Note the Parkinson's disease-associated lesions in both the limbic and the motor systems. Damaged structures are marked in deep red (severe lesions) or light red (less severe lesions). The diagrams are intended to facilitate an understanding of the functional consequences of the lesions (56)

Abbreviations: *AD* anterodorsal nucleus of the thalamus, *ant. cing. areas* anterior cingulate areas, *cereb. loop centres* cerebellar loop centres, *corp. gen. lat.* corpus geniculatum laterale, *corp. gen.med.* corpus geniculatum mediale, *diff. project. non-thal. Nucl.* Diffusely projecting non-thalamic nuclei, *dors. mot. IX, X* dorsal motor area of the glossopharyngeal and vagal nerves, *dors. Striatum* dorsal striatum, *hippoc. formation* hippocampal formation, *hypoth.*hypothalamus, *inf. oliv.* inferior olive, *m. b.* mamillary body, *magnoc. bas. forebr.* magnocellular nuclei of the basal forebrain, *MD* mediodorsal nuclei of the thalamus, *n. ruber magno.* The magnocellular portion of the nucleus ruber, *n. ruber parv.* parvocellular portion of the nucleus ruber, *Nucl. sol. tr.* nuclei of the solitary tract, *parabrachial. Nucl.* parabrachial nuclei, *periaqued. grey* periaqueductal gray, *prim.(a) sens. fields*, primary sensory fields, *r.s.* retrosplenial region, *raphe nucl.* raphe nuclei, *s. nigra* substantia nigra, *secondary sens. fields* secondary sensory fields, *sensory assoc. areas* sensory association areas, *spinocerebellar. tract* spinocerebellar tract, *subst. nigra* substantia nigra, *subthal. Nucleus* subthalamic nucleus, *transentorh. region* transentorhinal region, *tuberomam. Nucl.* tuberomammillary nucleus, *VA* ventral anterior nuclei of the thalamus, *ventr. pallidum*

ventral pallidum, *ventr. tegm.* ventral tegmentum, *VI* ventral intermediate nuclei of the thalamus, *VP* ventral posterior complex of the thalamus, *VIII* vestibular nerve

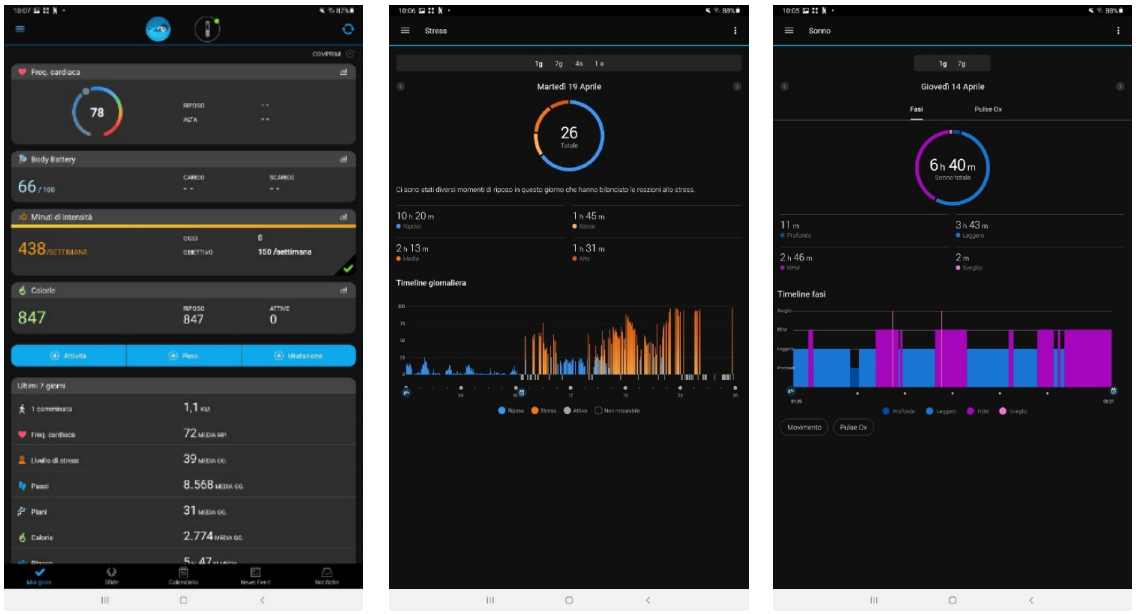


Figure 4. Garmin Connect app

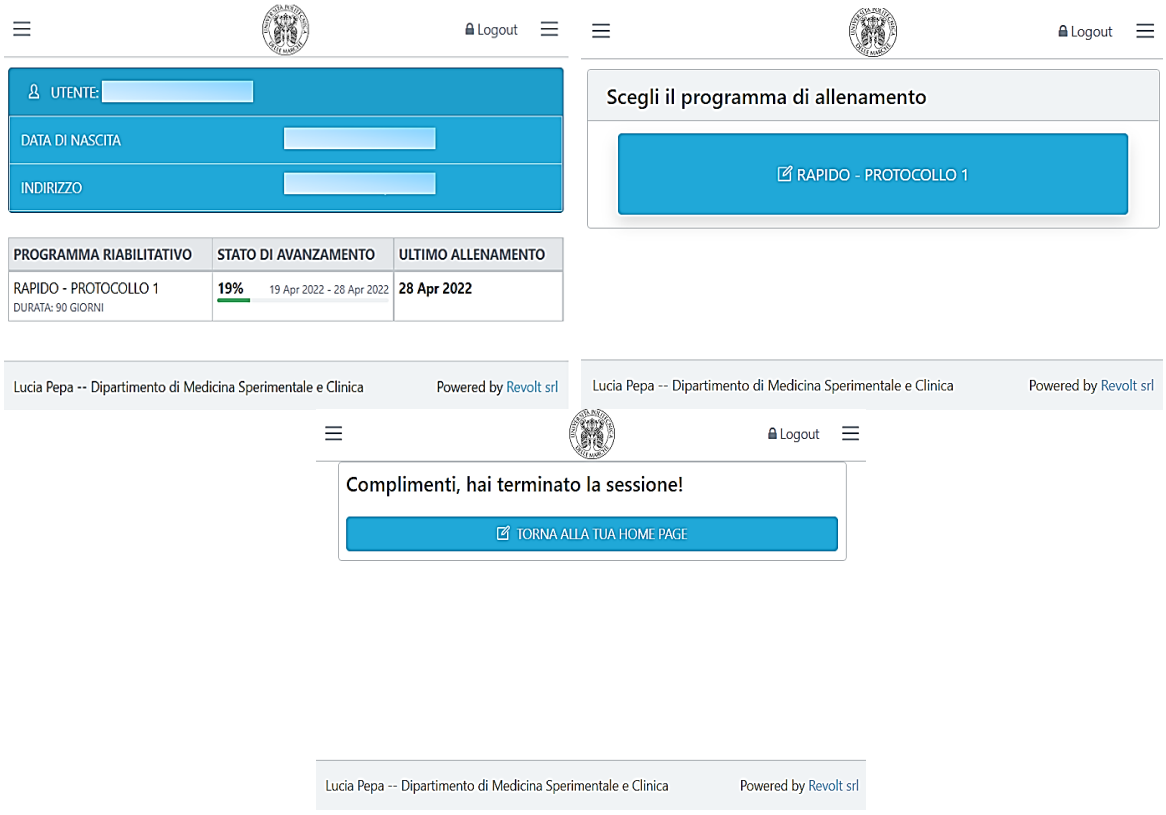
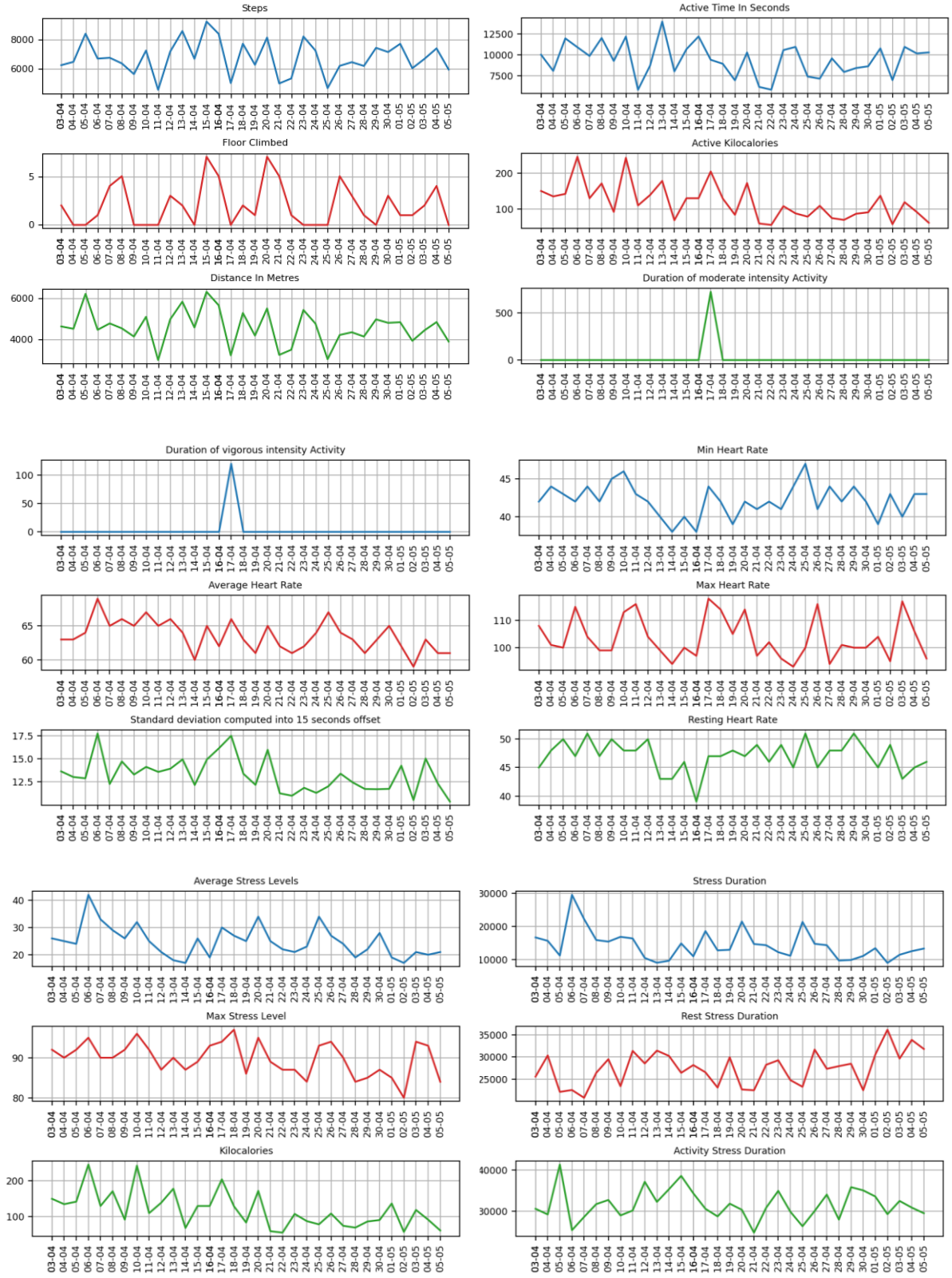


Figure 5. Rehabilitation platform: a. Progress of the rehabilitation protocol; b. Patient rehabilitation protocol; c. End of exercise session


Steps
Active Time In Seconds
Floor Climbed
Active Kilocalories
Distance In Metres
Duration of moderate intensity Activity
Duration of vigorous intensity Activity
Min Heart Rate
Average Heart Rate
Max Heart Rate
Standard deviation computed into 15 seconds offset
Resting Heart Rate
Average Stress Levels
Stress Duration
Max Stress Level
Rest Stress Duration
Kilocalories
Activity Stress Duration

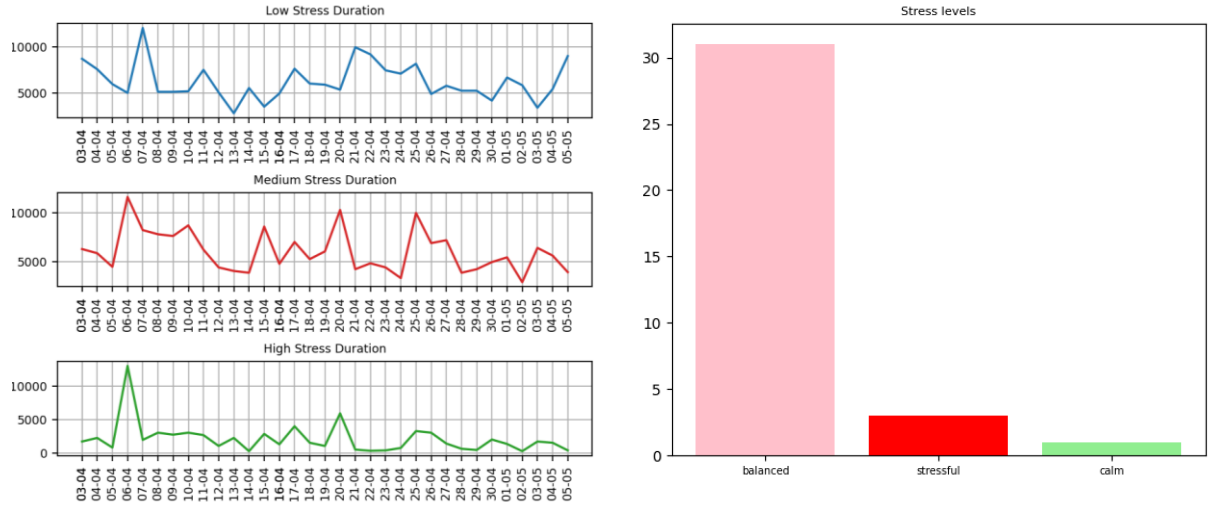


Figure 6. Dailies summaries plot – Subj 1

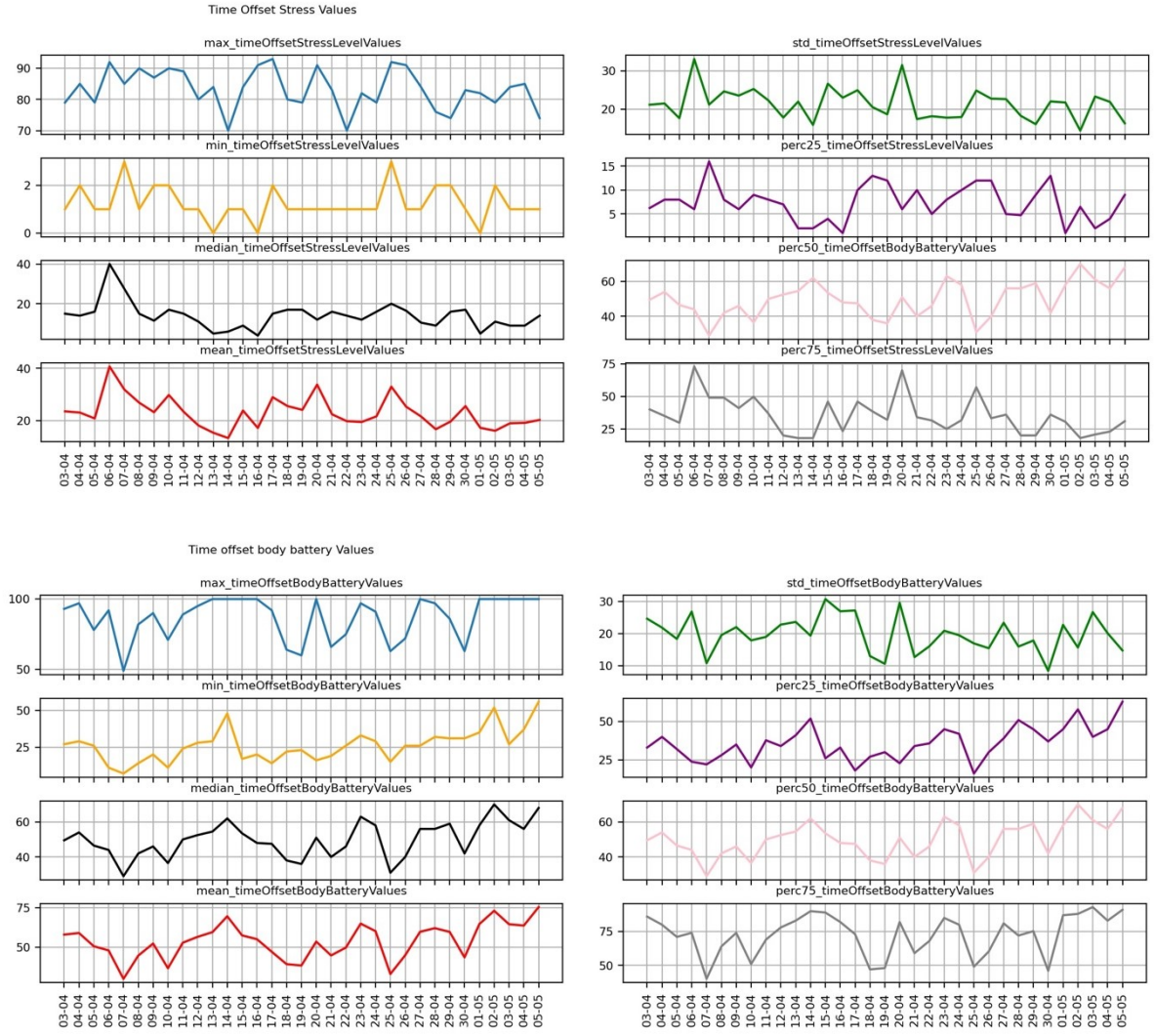


Figure 7. Stress summaries plot – Subj 1

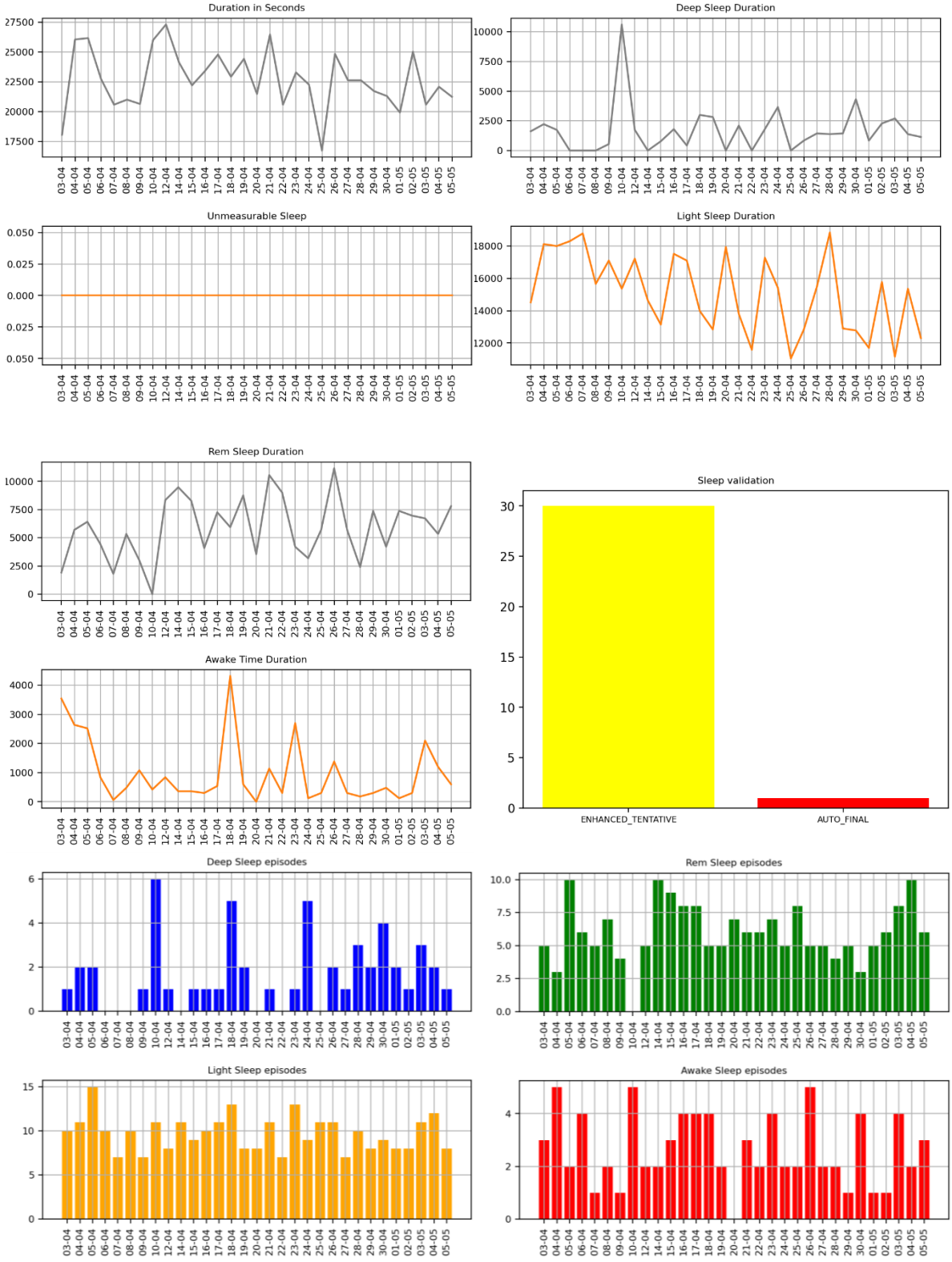


Figure 8. Sleep summary plot – Subj 1

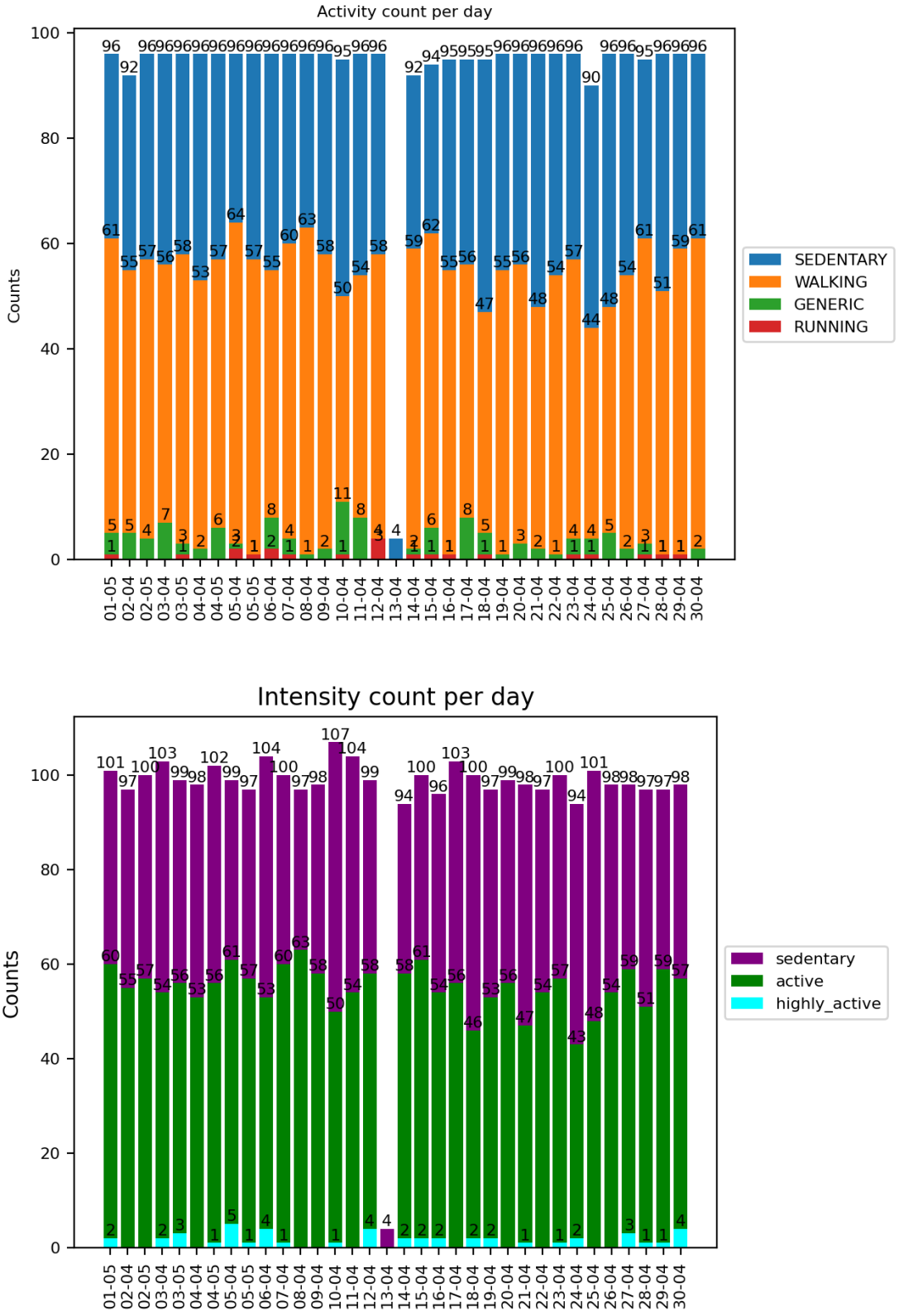
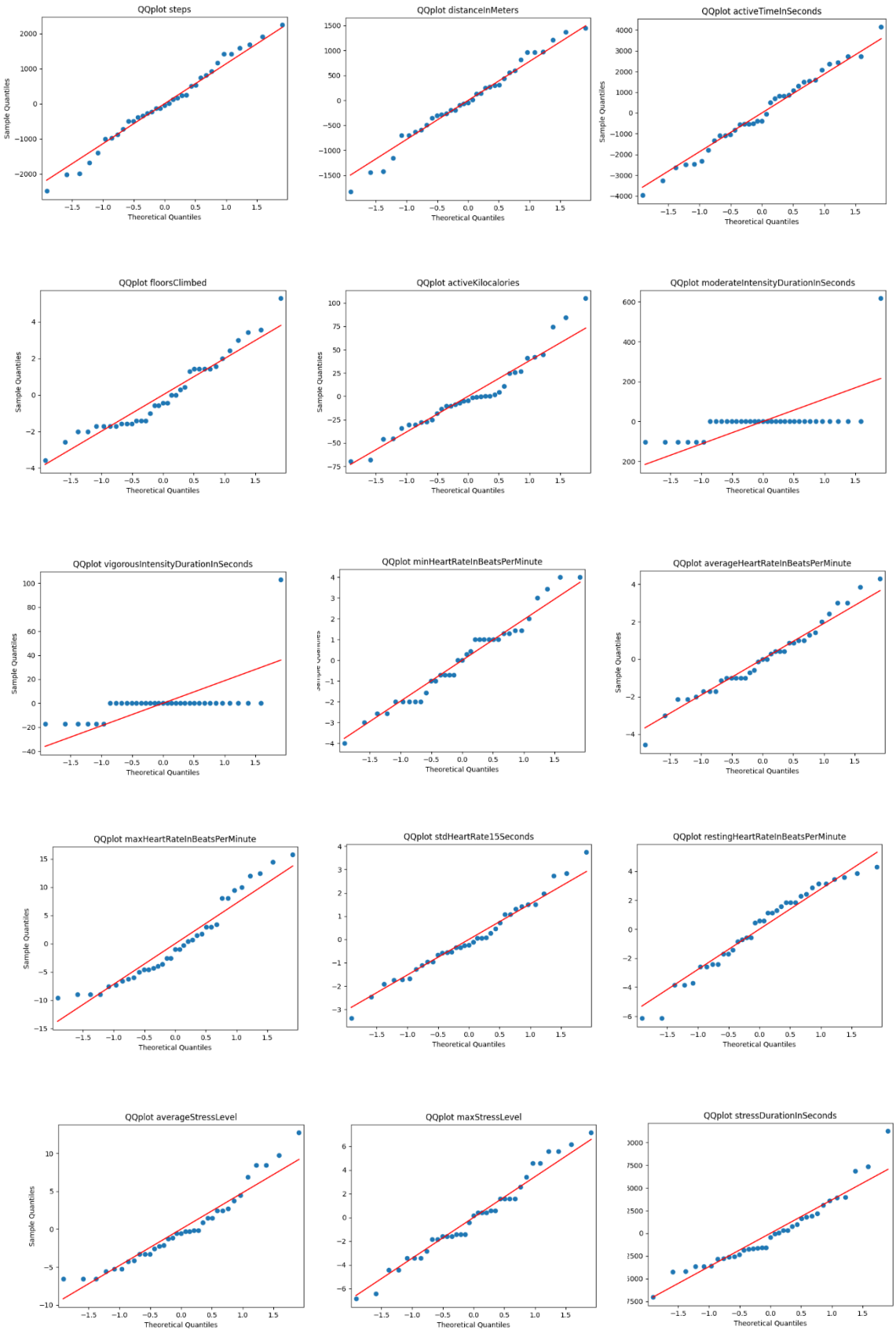


Figure 9. Epochs summaries plot – Subj 1


QQplot steps
QQplot distanceInMeters
QQplot activeTimeInSeconds
QQplot floorsClimbed
QQplot activeKilocalories
QQplot moderateIntensityDurationInSeconds
QQplot vigorousIntensityDurationInSeconds
QQplot minHeartRateInBeatsPerMinute
QQplot averageHeartRateInBeatsPerMinute
QQplot maxHeartRateInBeatsPerMinute
QQplot stdHeartRate15Seconds
QQplot restingHeartRateInBeatsPerMinute
QQplot averageStressLevel
QQplot maxStressLevel
QQplot stressDurationInSeconds
Sample Quantiles
Theoretical Quantiles

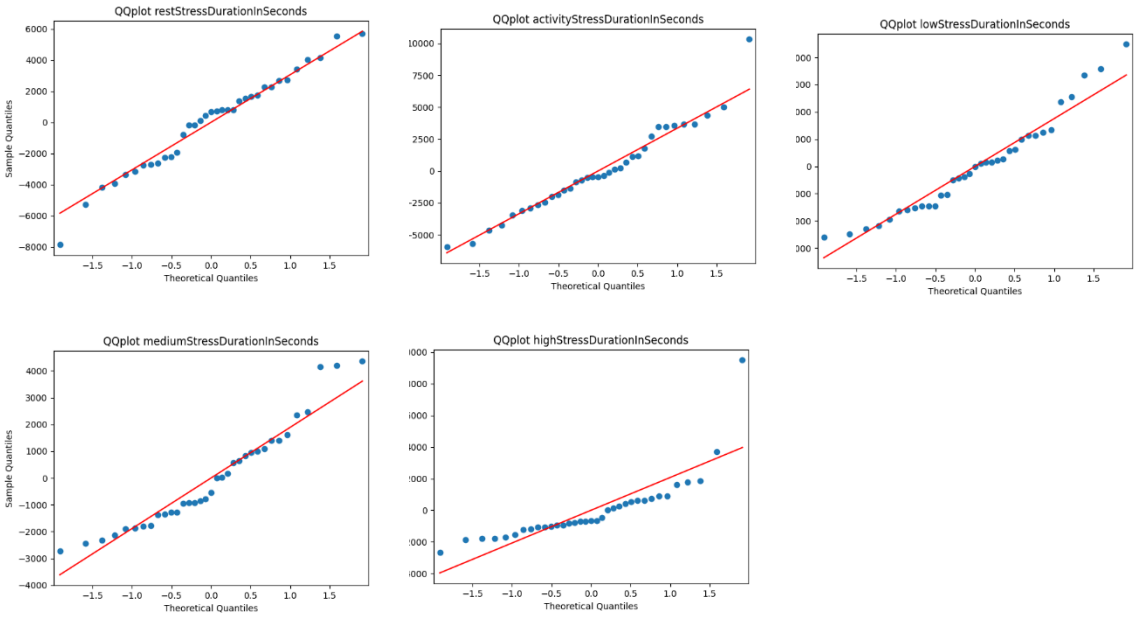
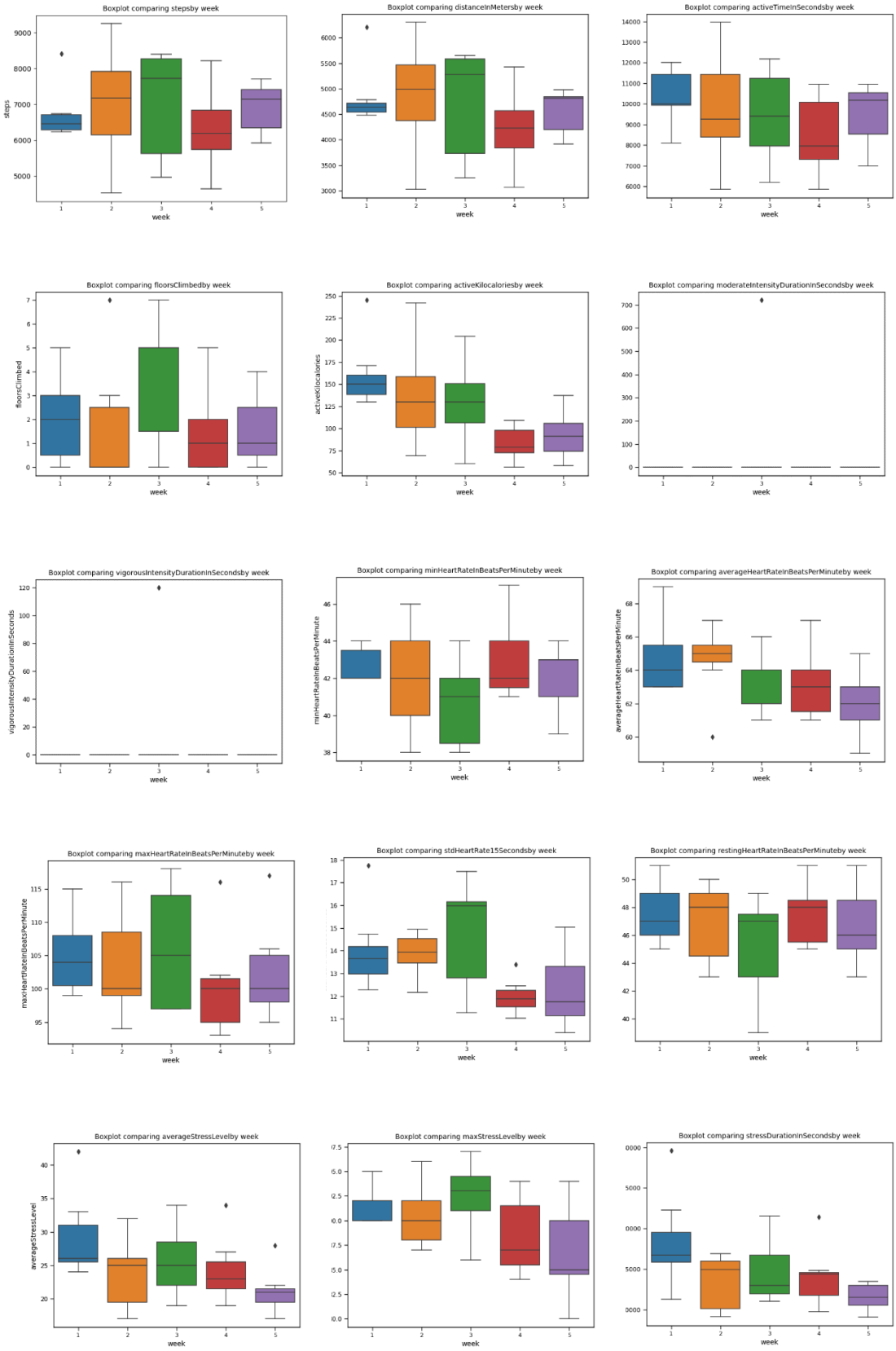


Figure 10. Dailies Quantile-quantile plot – Subj 1


Boxplot comparing stepsby week
steps
week
Boxplot comparing distanceInMetersby week
week
Boxplot comparing activeTimeInSecondsby week
week
Boxplot comparing floorsClimbedby week
floorsClimbed
week
Boxplot comparing activeKilocaloriesby week
activeKilocalories
week
Boxplot comparing moderateIntensityDurationInSecondsby week
week
Boxplot comparing vigorousIntensityDurationInSecondsby week
vigorousIntensityDurationInSeconds
week
Boxplot comparing minHeartRateInBeatsPerMinuteby week
minHeartRateInBeatsPerMinute
week
Boxplot comparing averageHeartRateInBeatsPerMinuteby week
averageHeartRateInBeatsPerMinute
week
Boxplot comparing maxHeartRateInBeatsPerMinuteby week
maxHeartRateInBeatsPerMinute
week
Boxplot comparing stdHeartRate15Secondsby week
week
Boxplot comparing restingHeartRateInBeatsPerMinuteby week
week
Boxplot comparing averageStressLevelby week
averageStressLevel
week
Boxplot comparing maxStressLevelby week
week
Boxplot comparing stressDurationInSecondsby week
week

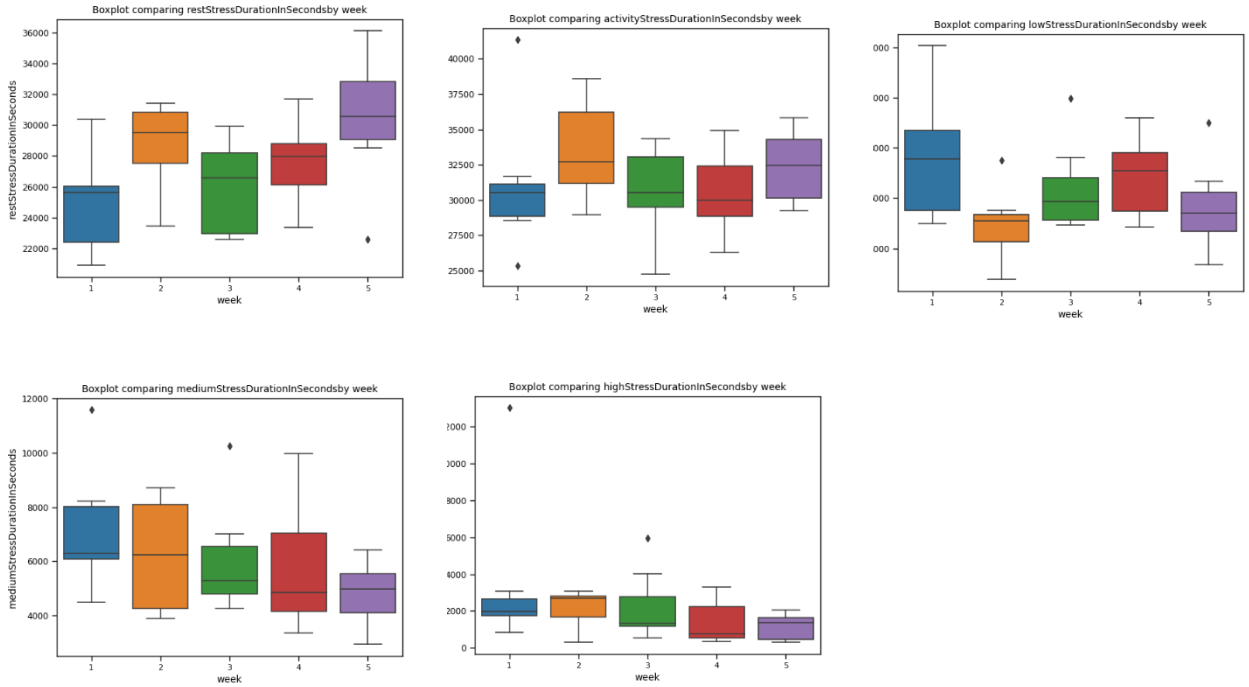


Figure 11. Dailies Box plot - Subj 1

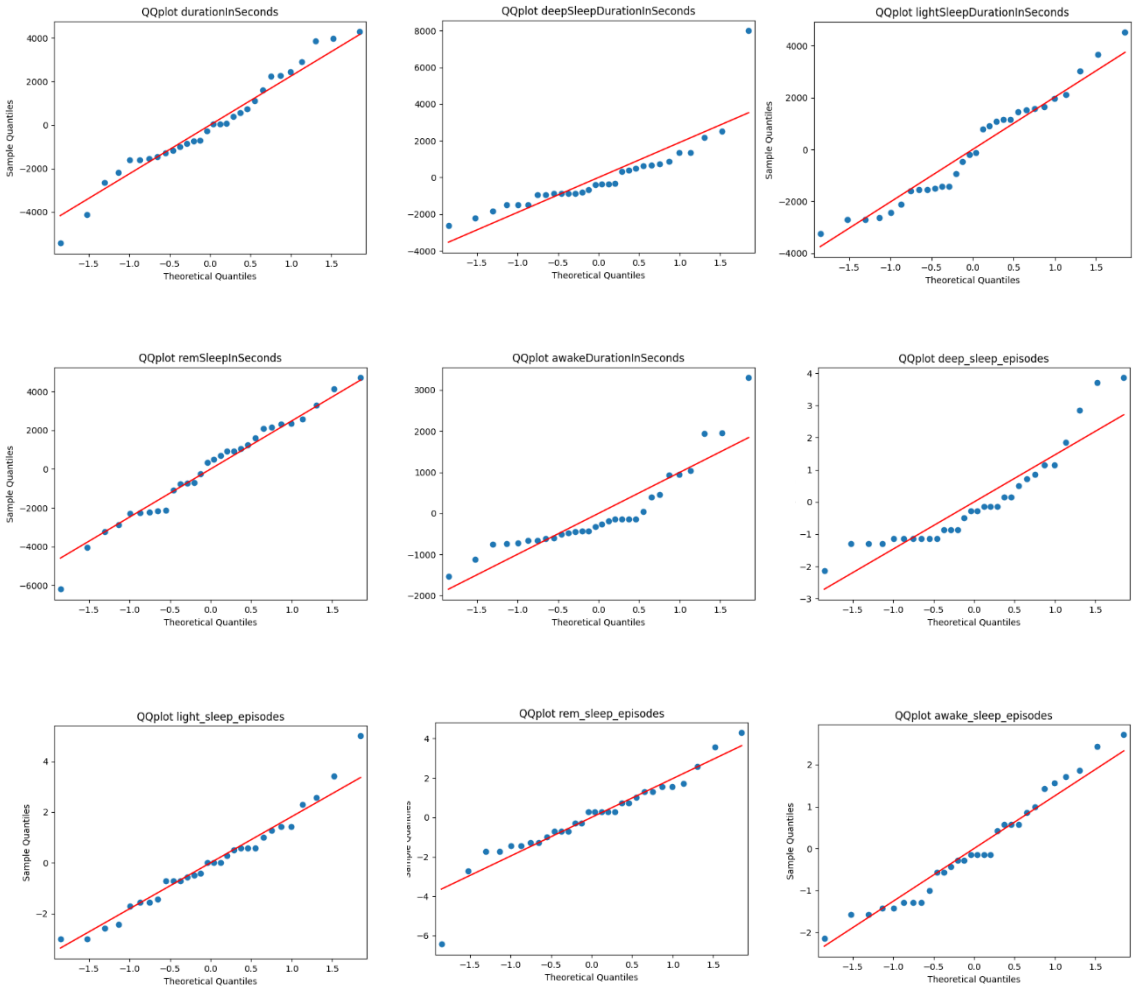


Figure 12. Sleep Quantile-quantile plot – Subj 1

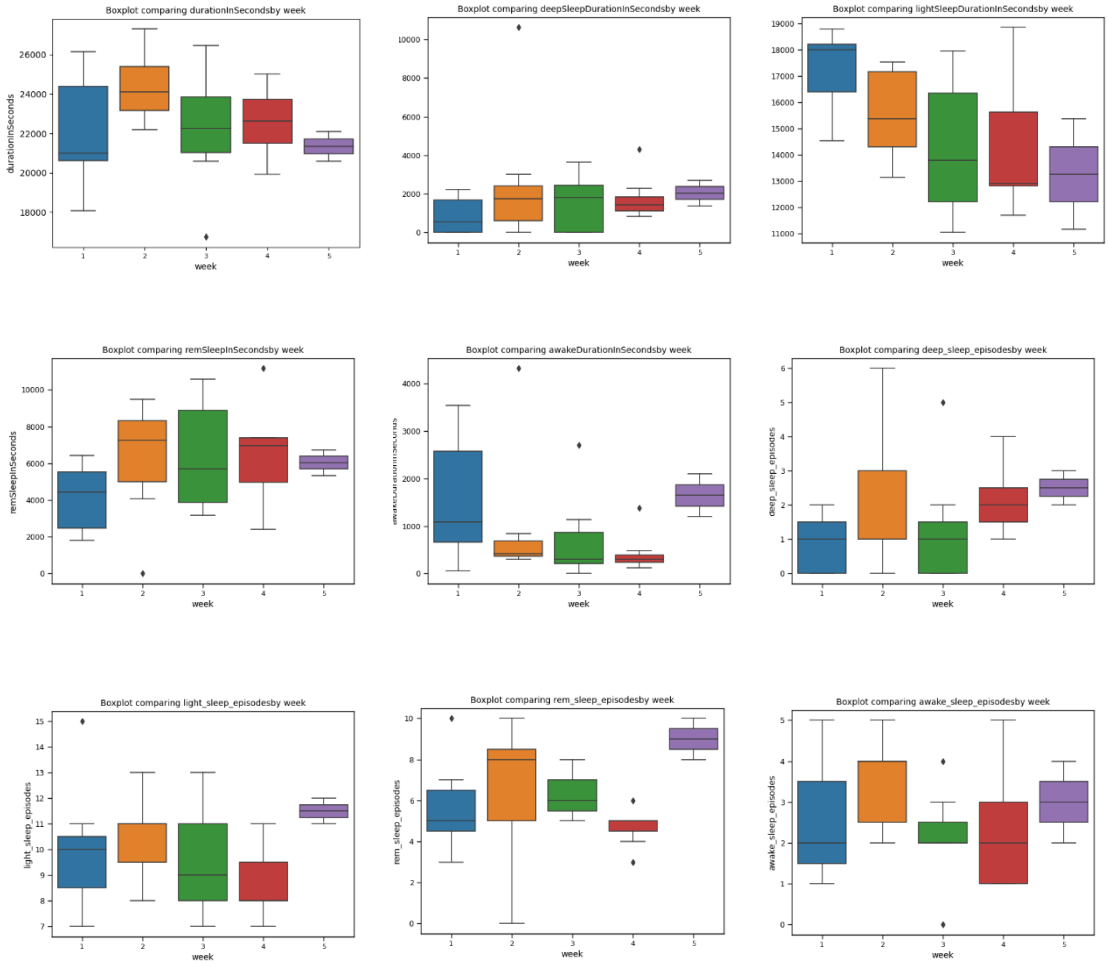
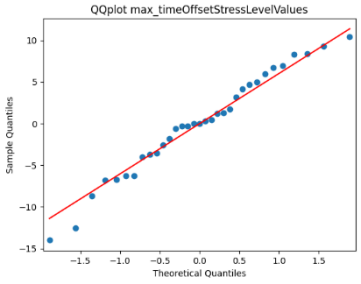
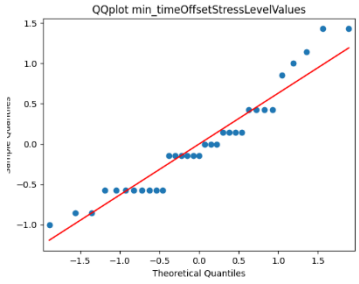
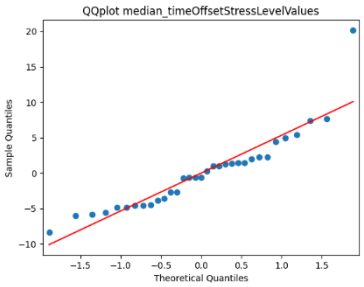
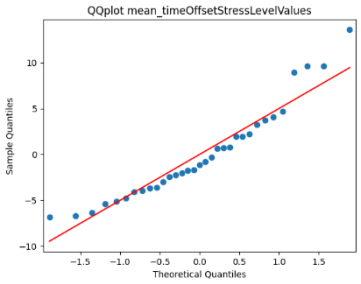


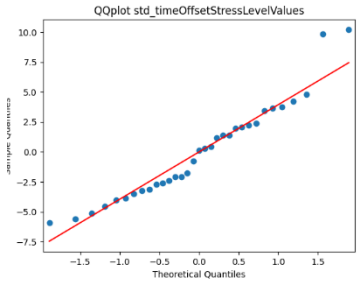
Figure 13. Sleep Box plot – Subj 1

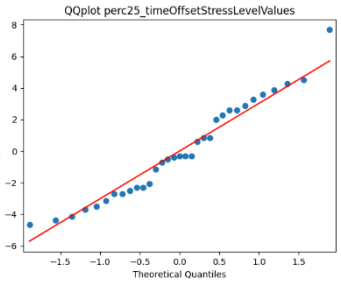

QQplot max_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

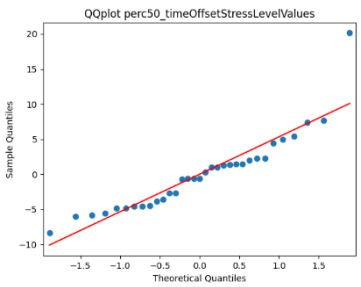

QQplot min_timeOffsetStressLevelValues
Theoretical Quantiles

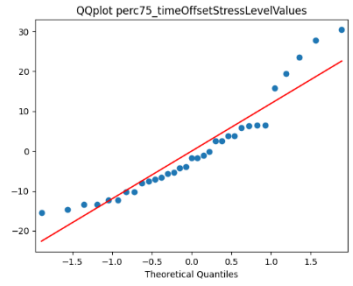

QQplot median_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

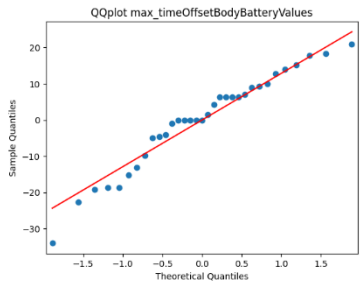

QQplot mean_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

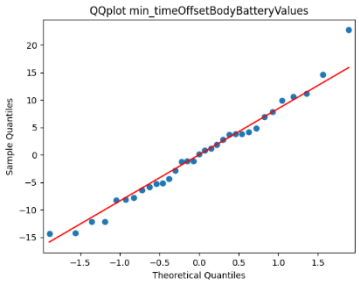

QQplot std_timeOffsetStressLevelValues
Theoretical Quantiles

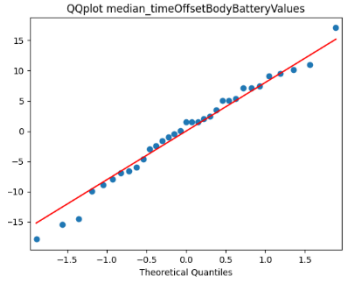

QQplot perc25_timeOffsetStressLevelValues
Theoretical Quantiles

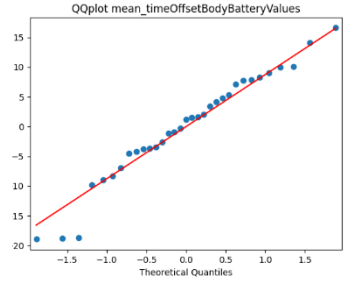

QQplot perc50_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

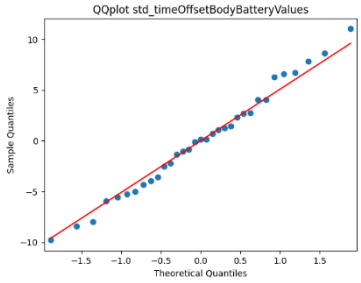

QQplot perc75_timeOffsetStressLevelValues
Theoretical Quantiles

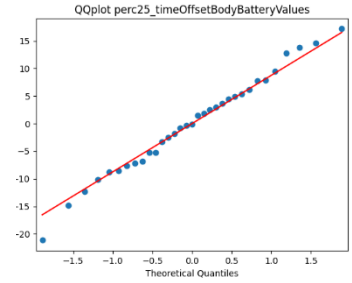

QQplot max_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles

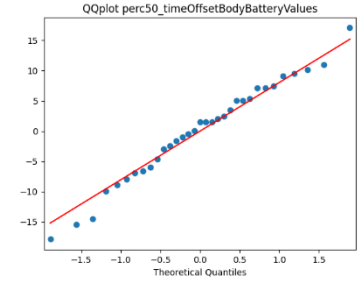

QQplot min_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles


QQplot median_timeOffsetBodyBatteryValues
Theoretical Quantiles


QQplot mean_timeOffsetBodyBatteryValues
Theoretical Quantiles


QQplot std_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles


QQplot perc25_timeOffsetBodyBatteryValues
Theoretical Quantiles


QQplot perc50_timeOffsetBodyBatteryValues
Theoretical Quantiles

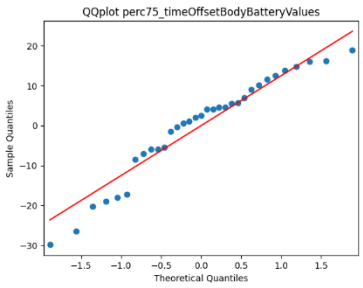
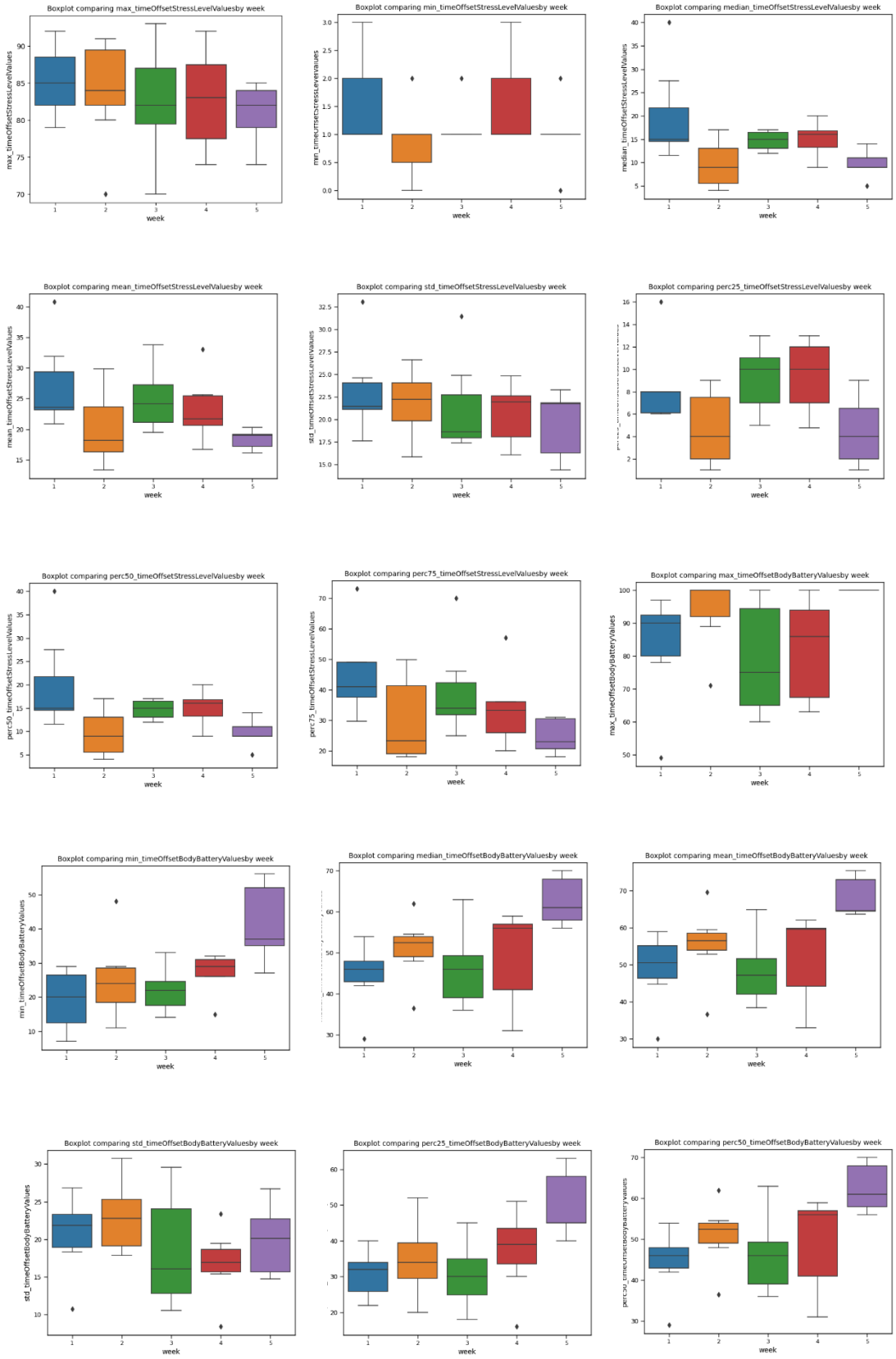


Figure 14. Stress Quantile-quantile plot – Subj 1


Boxplot comparing max_timeOffsetStressLevelValuesby week
max_timeOffsetStressLevelValues
week
Boxplot comparing min_timeOffsetStressLevelValuesby week
min_timeOffsetStressLevelValues
week
Boxplot comparing median_timeOffsetStressLevelValuesby week
median_timeOffsetStressLevelValues
week
Boxplot comparing mean_timeOffsetStressLevelValuesby week
mean_timeOffsetStressLevelValues
week
Boxplot comparing std_timeOffsetStressLevelValuesby week
std_timeOffsetStressLevelValues
week
Boxplot comparing perc25_timeOffsetStressLevelValuesby week
week
Boxplot comparing perc50_timeOffsetStressLevelValuesby week
perc50_timeOffsetStressLevelValues
week
Boxplot comparing perc75_timeOffsetStressLevelValuesby week
perc75_timeOffsetStressLevelValues
week
Boxplot comparing max_timeOffsetBodyBatteryValuesby week
max_timeOffsetBodyBatteryValues
week
Boxplot comparing min_timeOffsetBodyBatteryValuesby week
min_timeOffsetBodyBatteryValues
week
Boxplot comparing median_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing mean_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing std_timeOffsetBodyBatteryValuesby week
std_timeOffsetBodyBatteryValues
week
Boxplot comparing perc25_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing perc50_timeOffsetBodyBatteryValuesby week
week

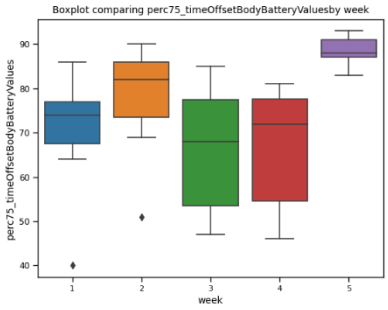
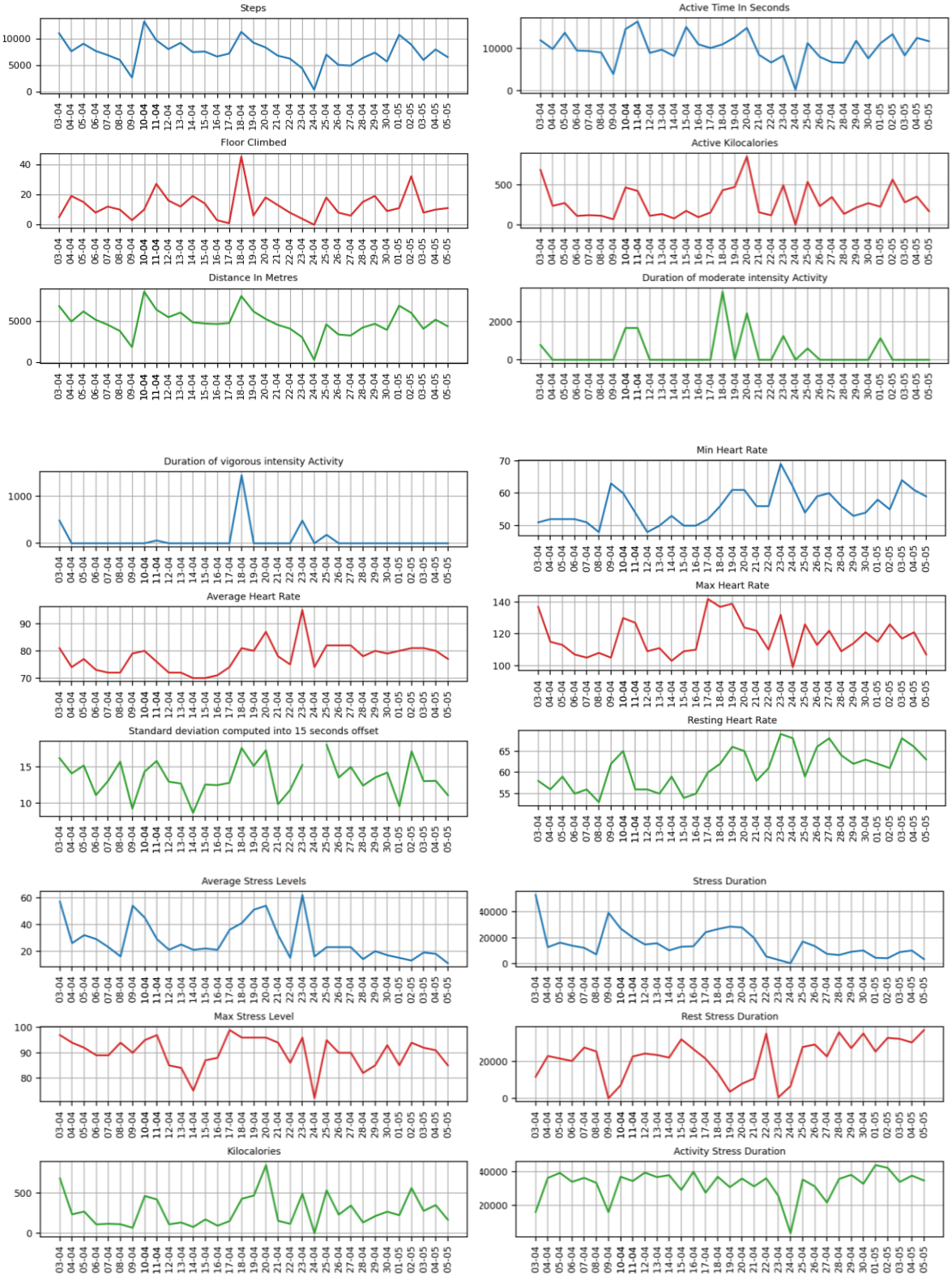


Figure 15. Stress Box plot – Subj 1


Steps
Active Time In Seconds
Floor Climbed
Active Kilocalories
Distance In Metres
Duration of moderate intensity Activity
Duration of vigorous intensity Activity
Min Heart Rate
Average Heart Rate
Max Heart Rate
Standard deviation computed into 15 seconds offset
Resting Heart Rate
Average Stress Levels
Stress Duration
Max Stress Level
Rest Stress Duration
Kilocalories
Activity Stress Duration

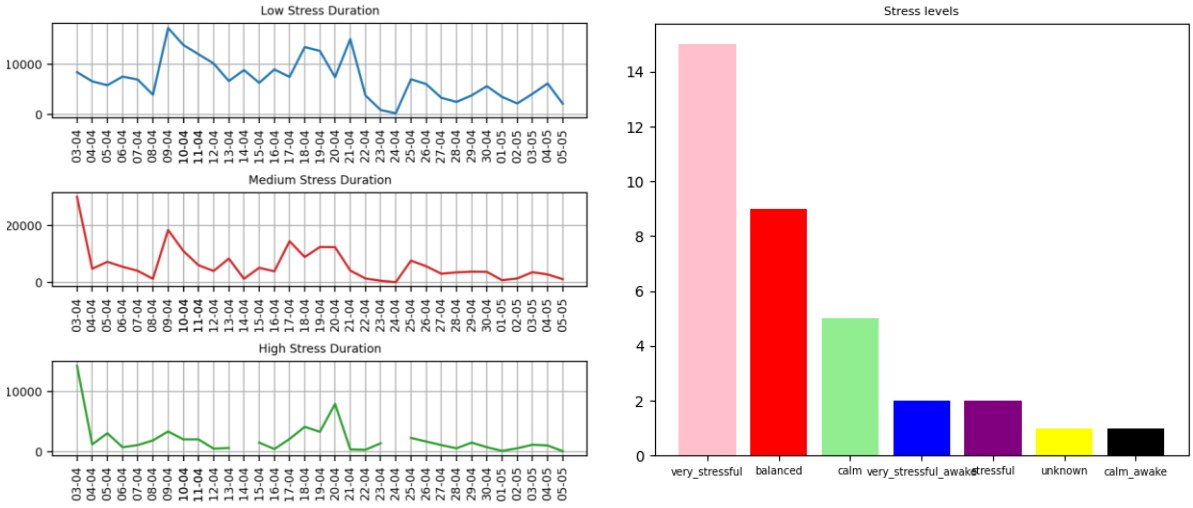


Figure 16 Dailies summaries plot – Subj 2

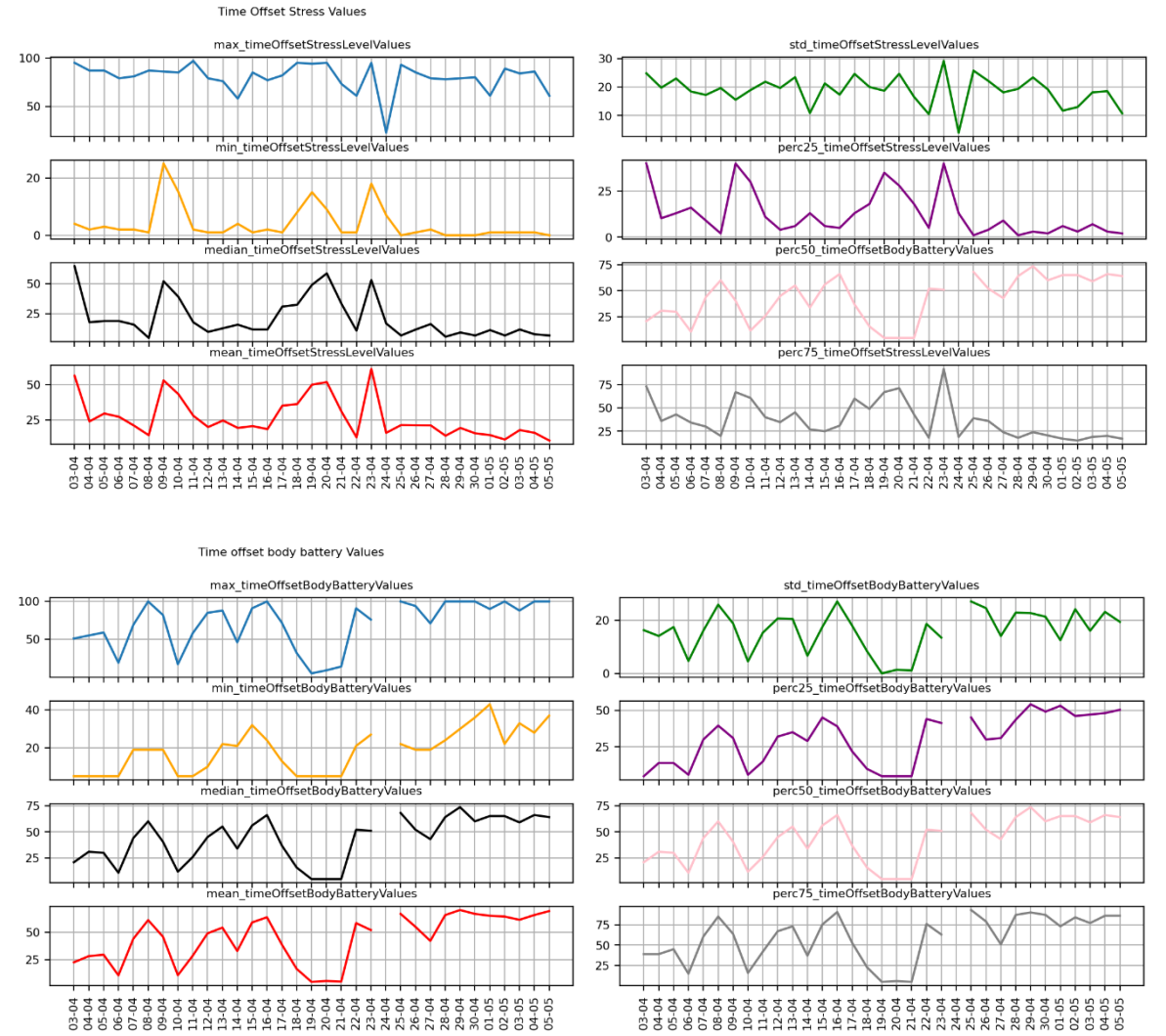


Figure 17 Stress summaries plot – Subj 2

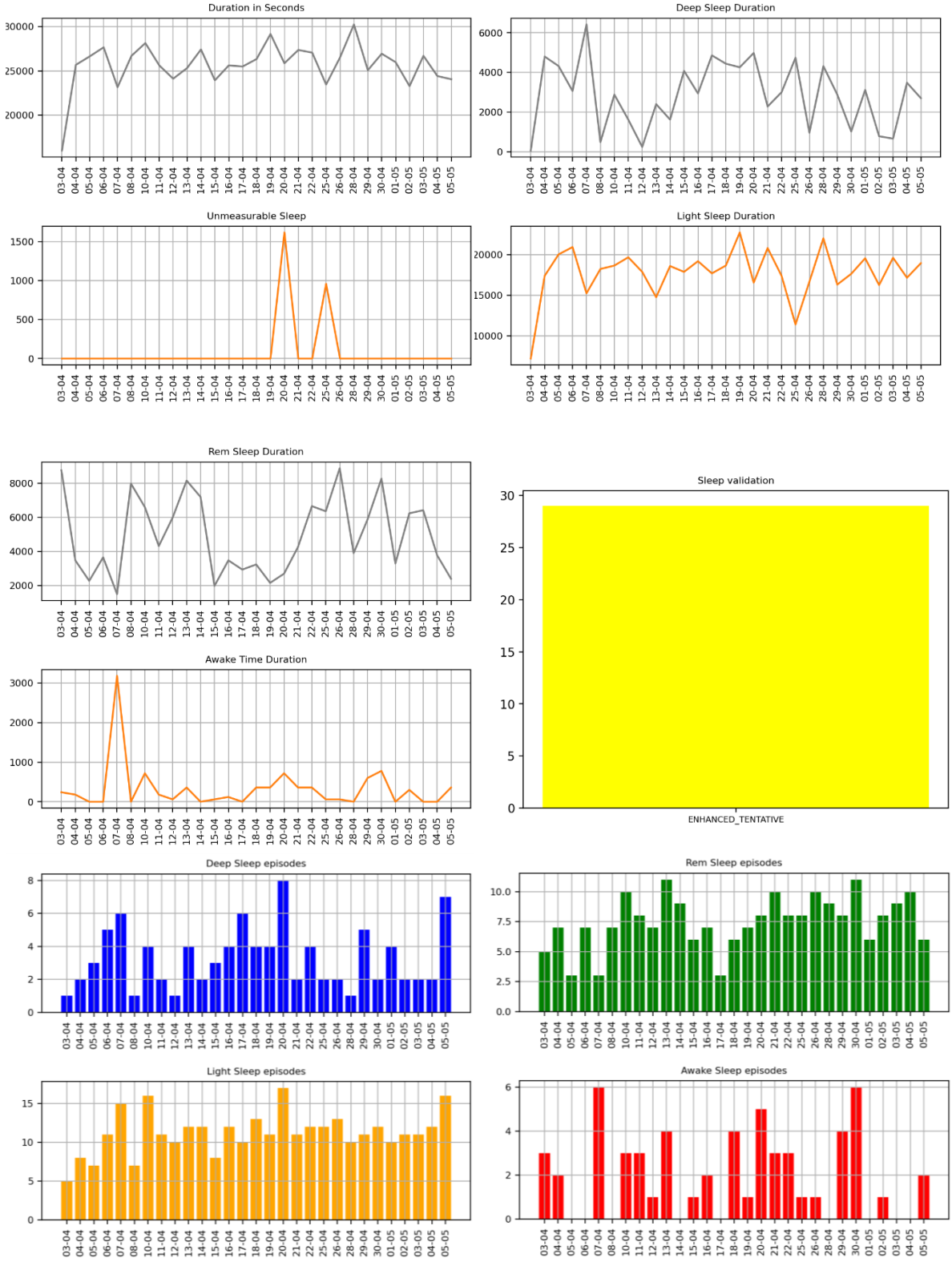


Figure 18 Sleep summary plot – Subj 2

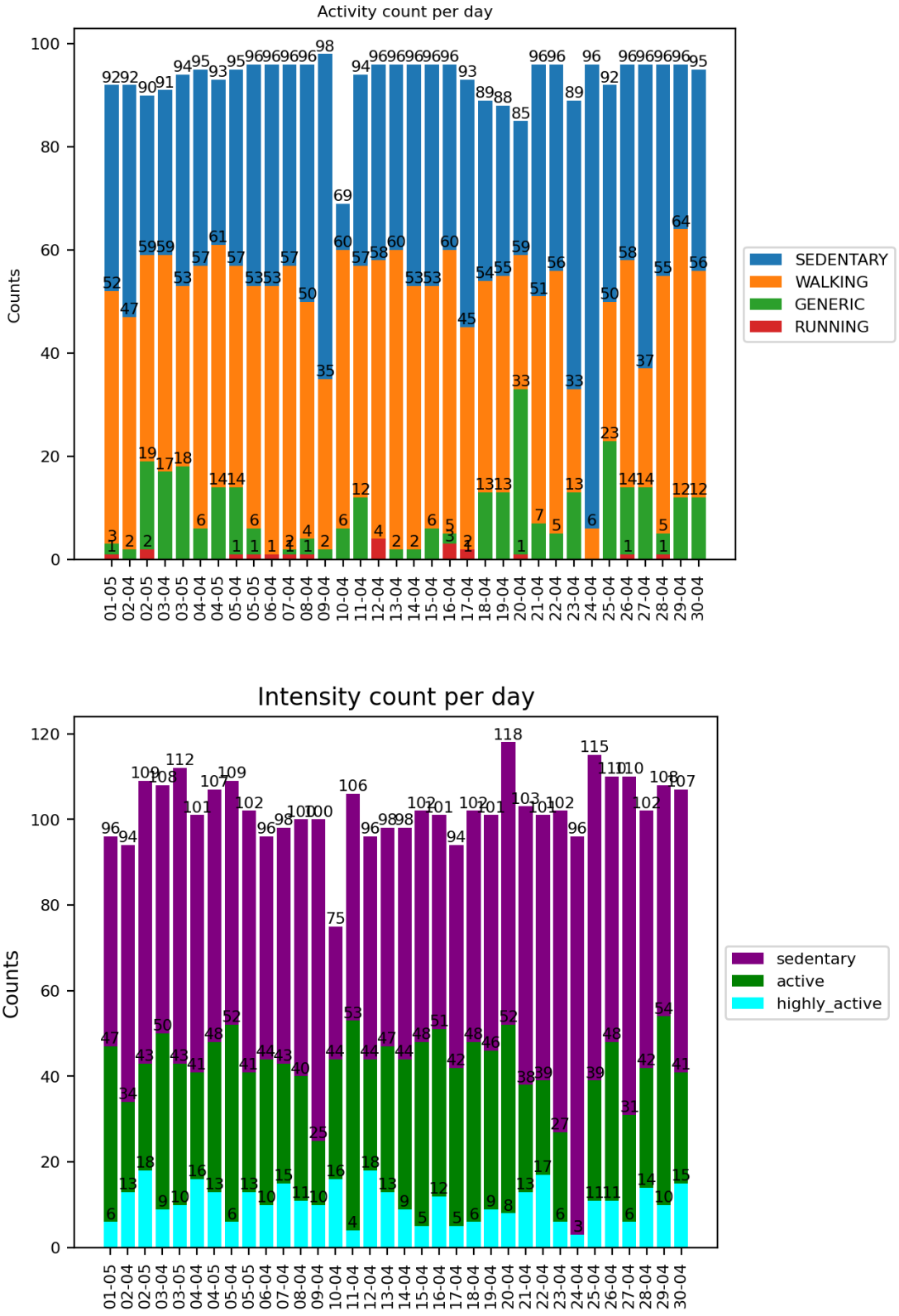
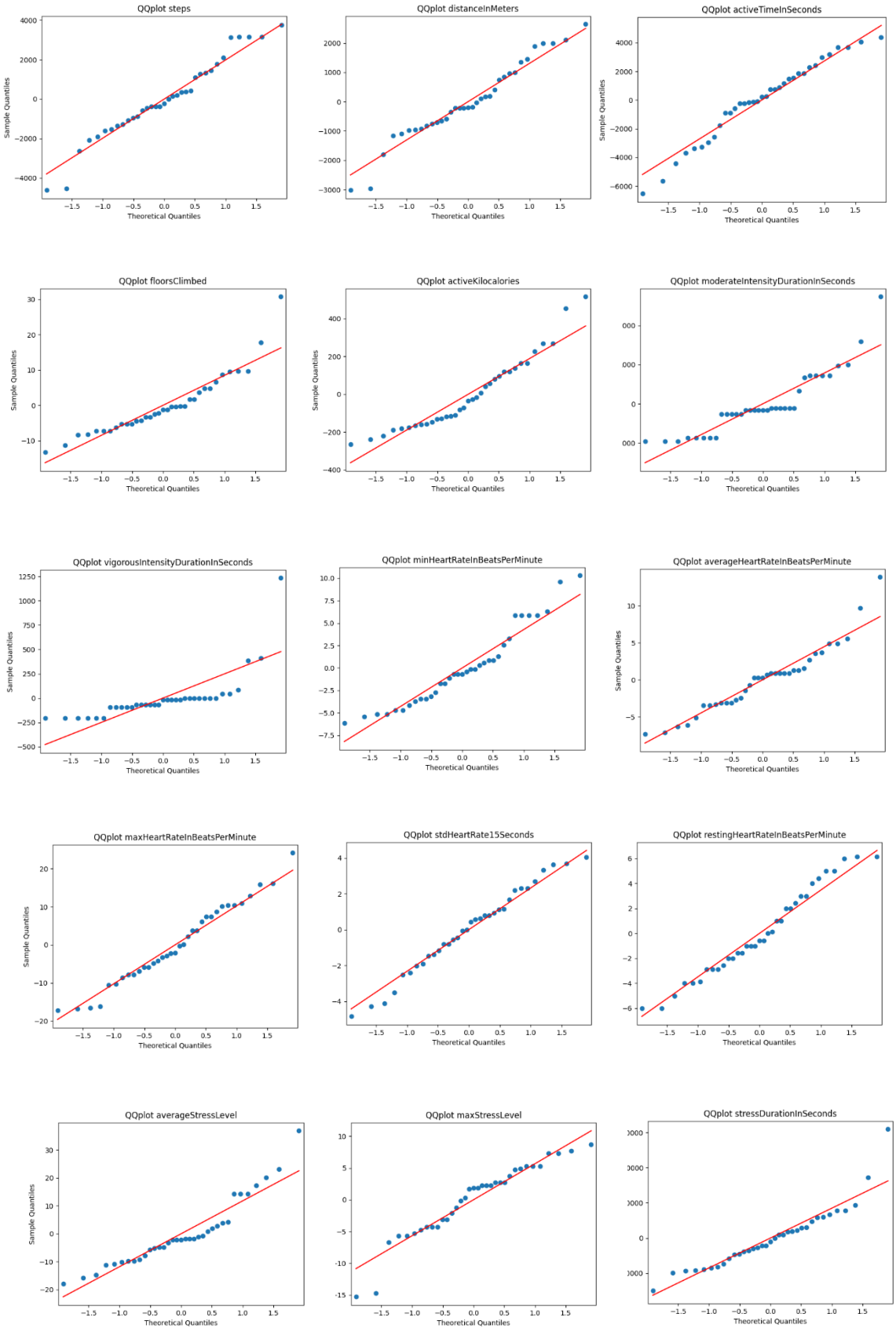


Figure 19 Epochs summaries plot – Subj 2


QQplot steps
QQplot distanceInMeters
QQplot activeTimeInSeconds
QQplot floorsClimbed
QQplot activeKilocalories
QQplot moderateIntensityDurationInSeconds
QQplot vigorousIntensityDurationInSeconds
QQplot minHeartRateInBeatsPerMinute
QQplot averageHeartRateInBeatsPerMinute
QQplot maxHeartRateInBeatsPerMinute
QQplot stdHeartRate15Seconds
QQplot restingHeartRateInBeatsPerMinute
QQplot averageStressLevel
QQplot maxStressLevel
QQplot stressDurationInSeconds
Sample Quantiles
Theoretical Quantiles

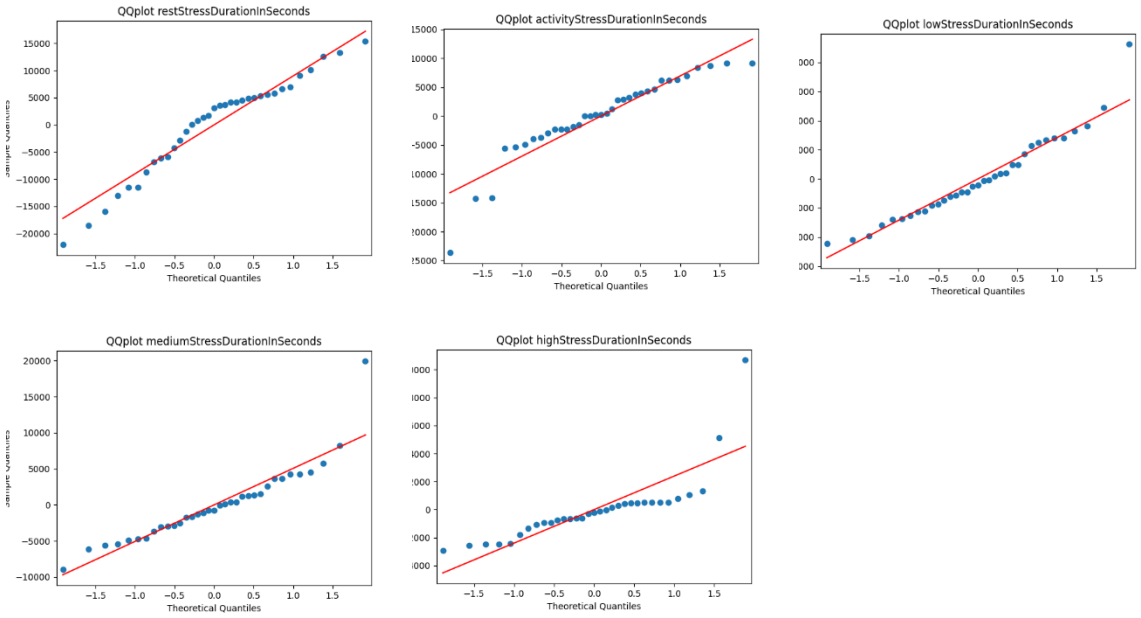
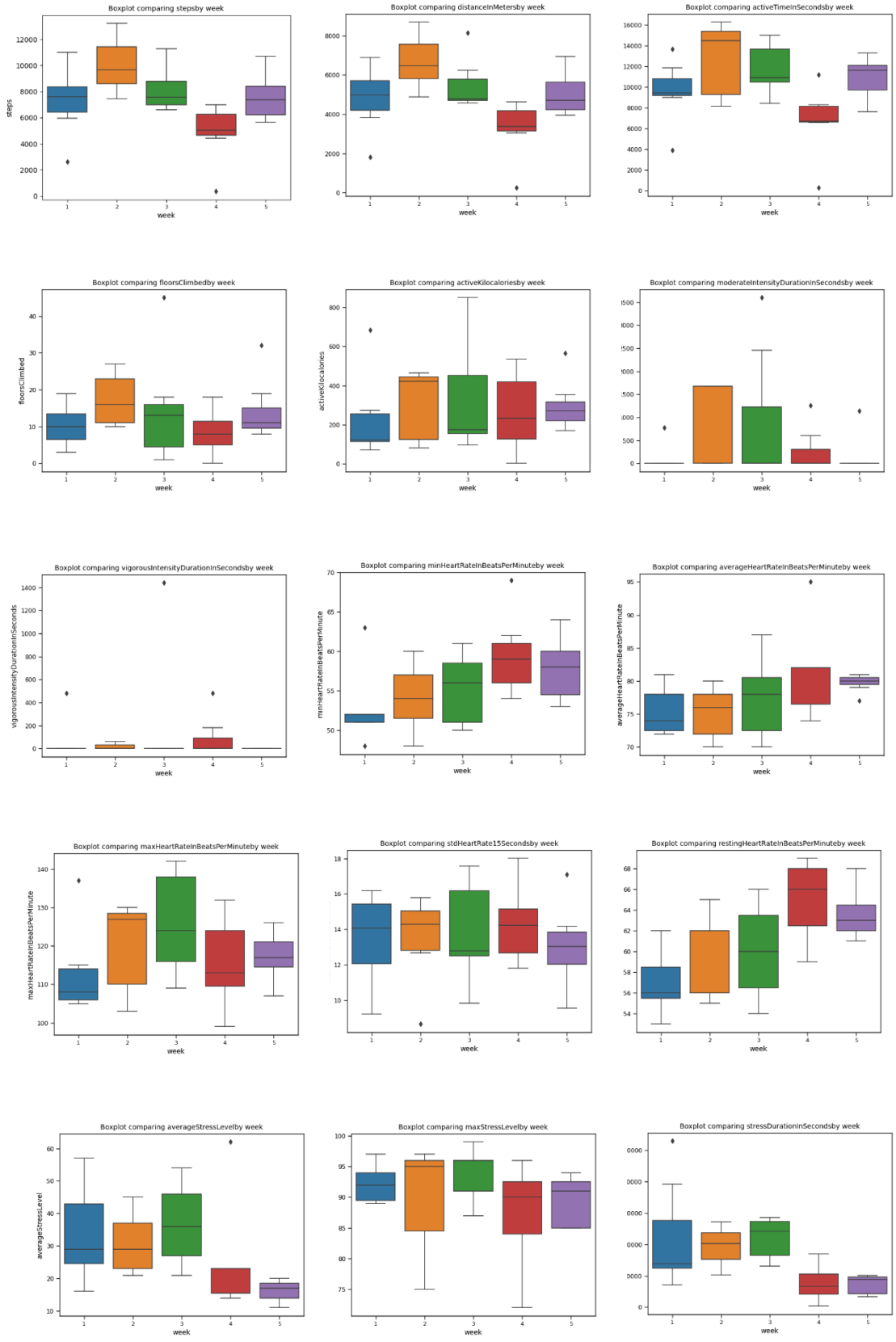


Figure 20 Dailies Quantile-quantile plot – Subj 2


Boxplot comparing stepsby week
steps
week
Boxplot comparing distanceInMetersby week
week
Boxplot comparing activeTimeInSecondsby week
week
Boxplot comparing floorsClimbedby week
floorsClimbed
week
Boxplot comparing activeKilocaloriesby week
activeKilocalories
week
Boxplot comparing moderateIntensityDurationInSecondsby week
week
Boxplot comparing vigorousIntensityDurationInSecondsby week
vigorousIntensityDurationInSeconds
week
Boxplot comparing minHeartRateInBeatsPerMinuteby week
minHeartRateInBeatsPerMinute
week
Boxplot comparing averageHeartRateInBeatsPerMinuteby week
averageHeartRateInBeatsPerMinute
week
Boxplot comparing maxHeartRateInBeatsPerMinuteby week
maxHeartRateInBeatsPerMinute
week
Boxplot comparing stdHeartRate15Secondsby week
week
Boxplot comparing restingHeartRateInBeatsPerMinuteby week
week
Boxplot comparing averageStressLevelby week
averageStressLevel
week
Boxplot comparing maxStressLevelby week
week
Boxplot comparing stressDurationInSecondsby week
week

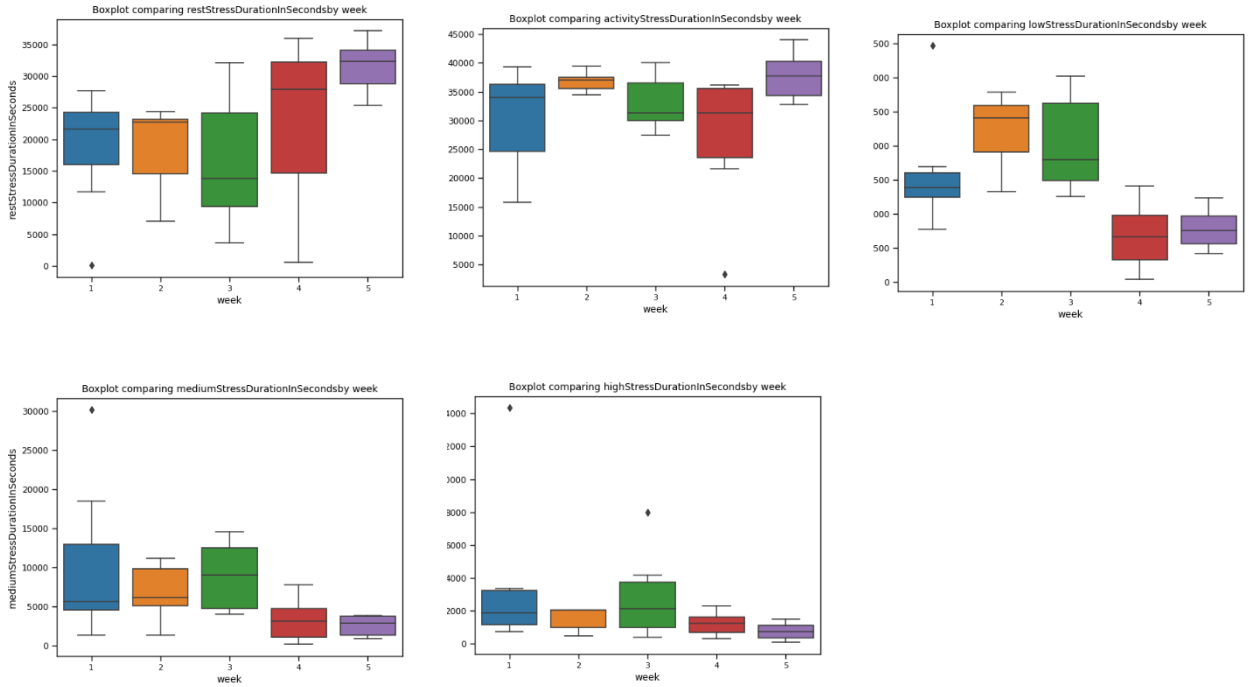


Figure 21 Dailies Box plot - Subj 2

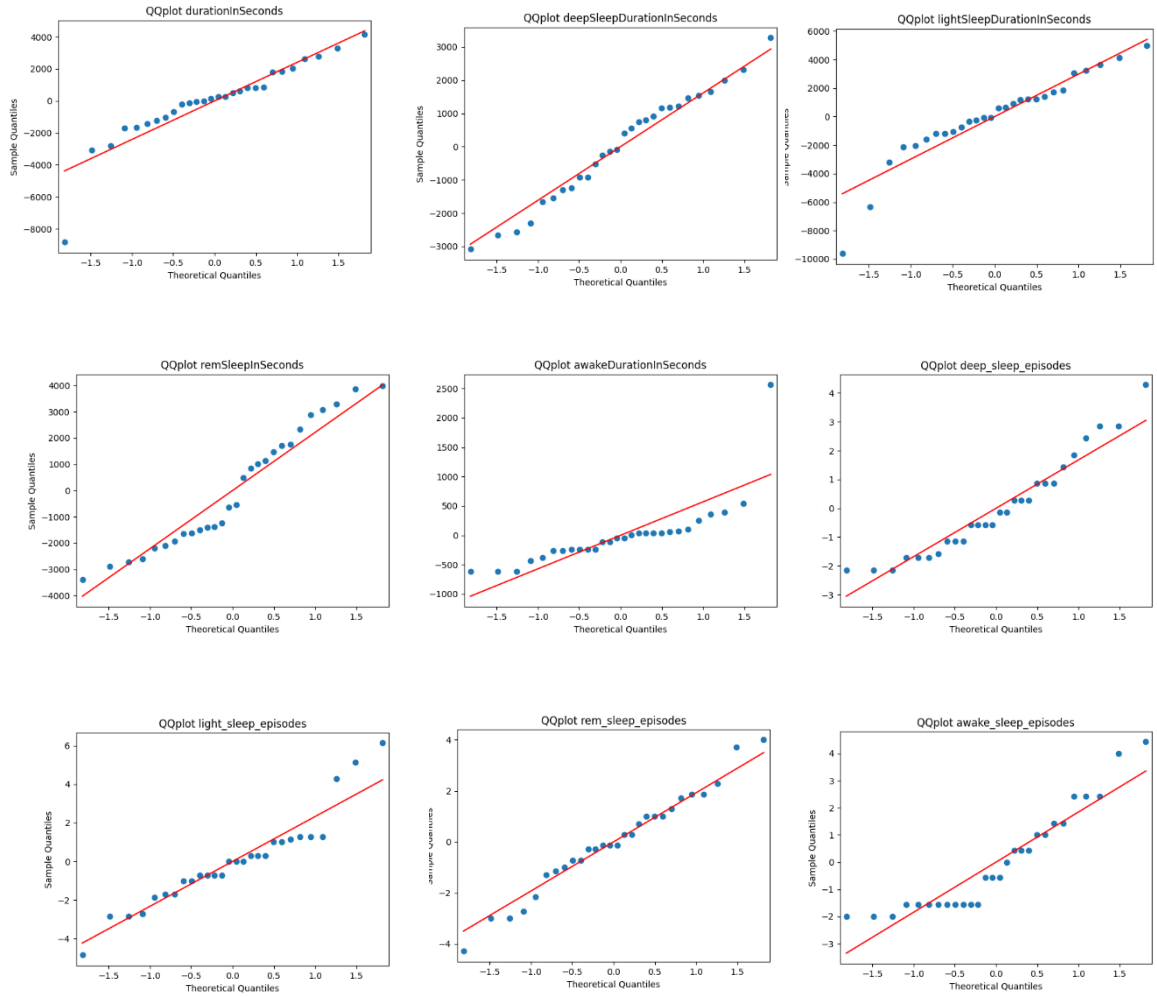


Figure 22 Sleep Quantile-quantile plot – Subj 2

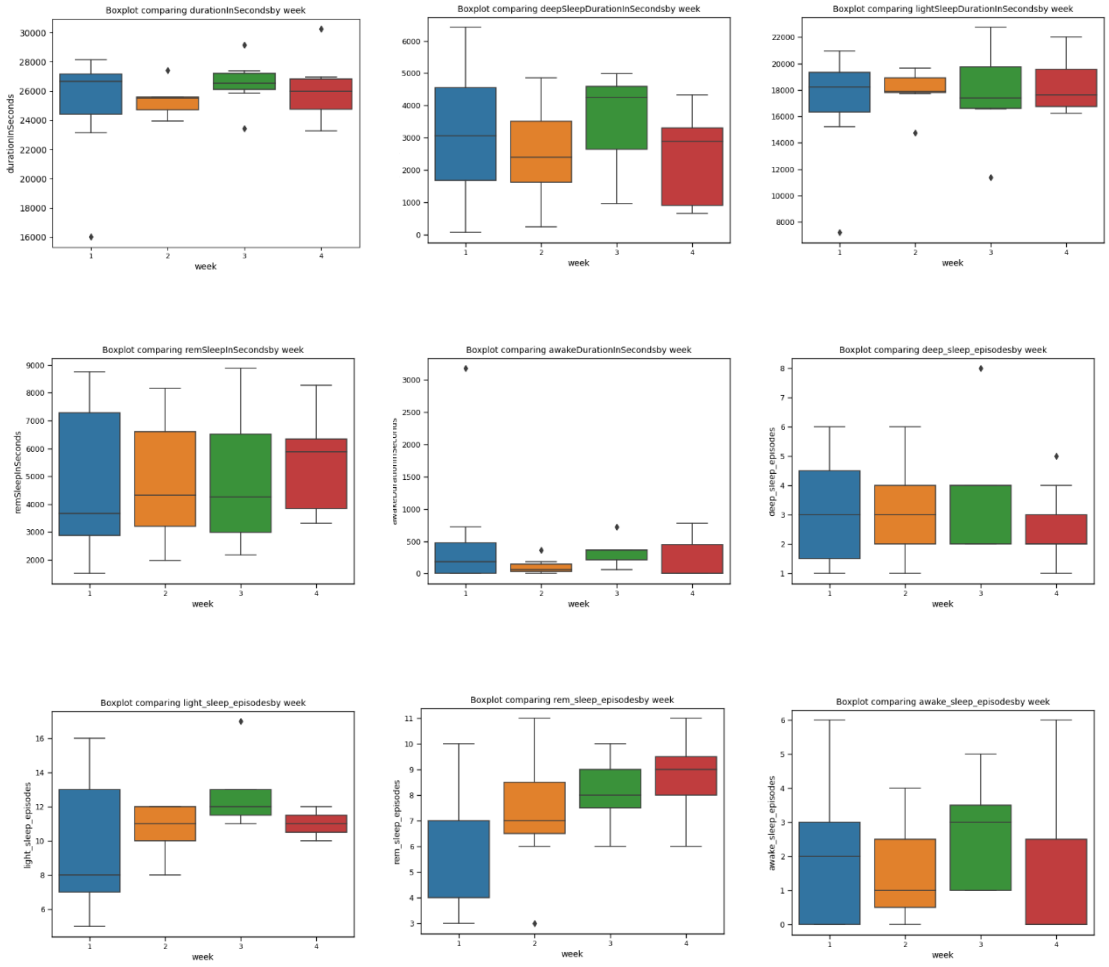
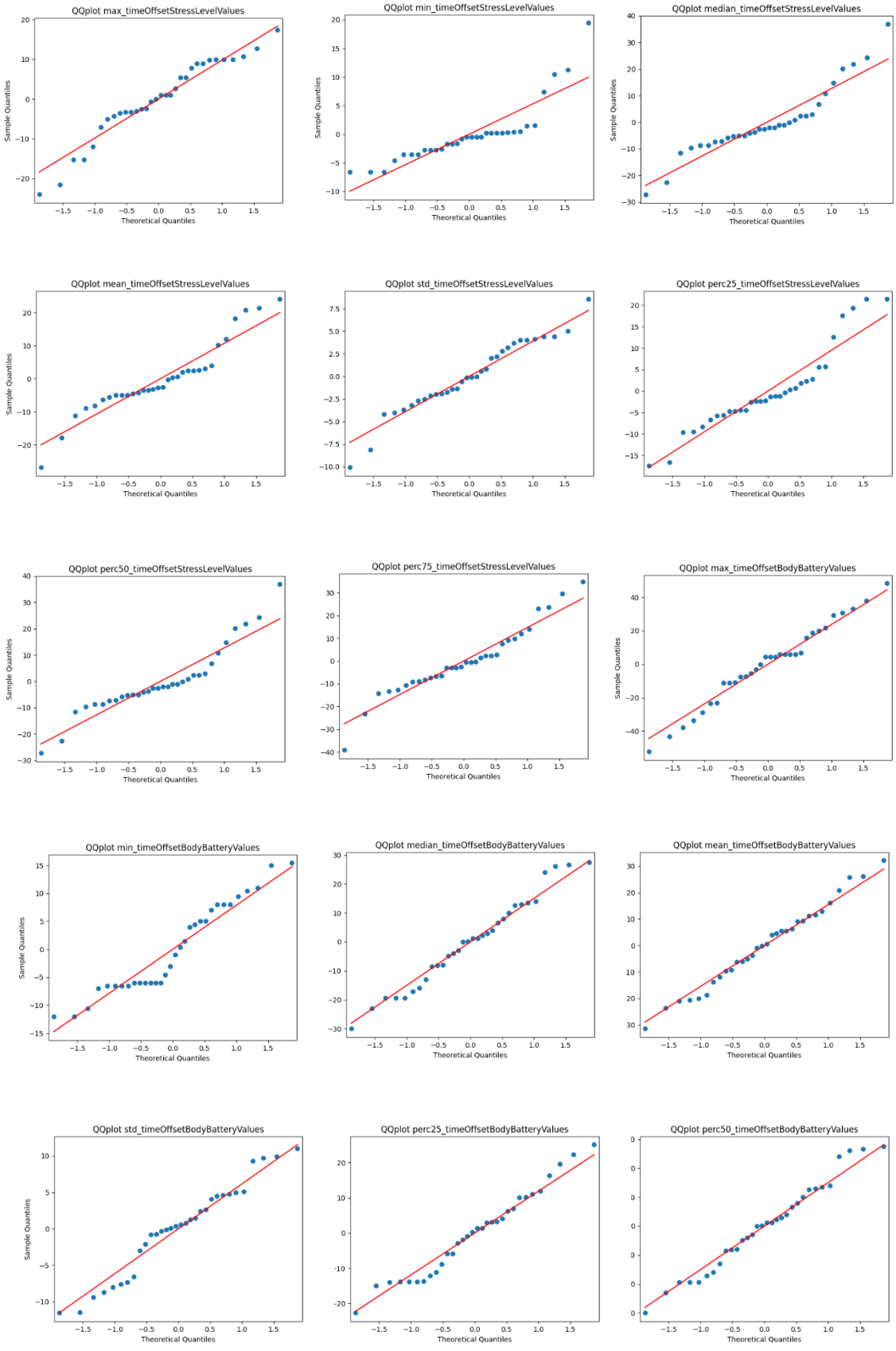


Figure 23 Sleep Box plot – Subj 2


QQplot max_timeOffsetStressLevelValues
QQplot min_timeOffsetStressLevelValues
QQplot median_timeOffsetStressLevelValues
QQplot mean_timeOffsetStressLevelValues
QQplot std_timeOffsetStressLevelValues
QQplot perc25_timeOffsetStressLevelValues
QQplot perc50_timeOffsetStressLevelValues
QQplot perc75_timeOffsetStressLevelValues
QQplot max_timeOffsetBodyBatteryValues
QQplot min_timeOffsetBodyBatteryValues
QQplot median_timeOffsetBodyBatteryValues
QQplot mean_timeOffsetBodyBatteryValues
QQplot std_timeOffsetBodyBatteryValues
QQplot perc25_timeOffsetBodyBatteryValues
QQplot perc50_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles

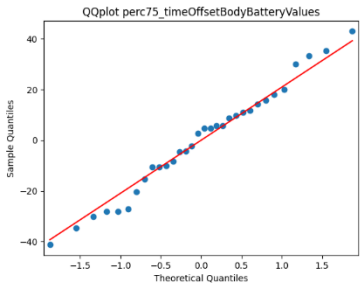
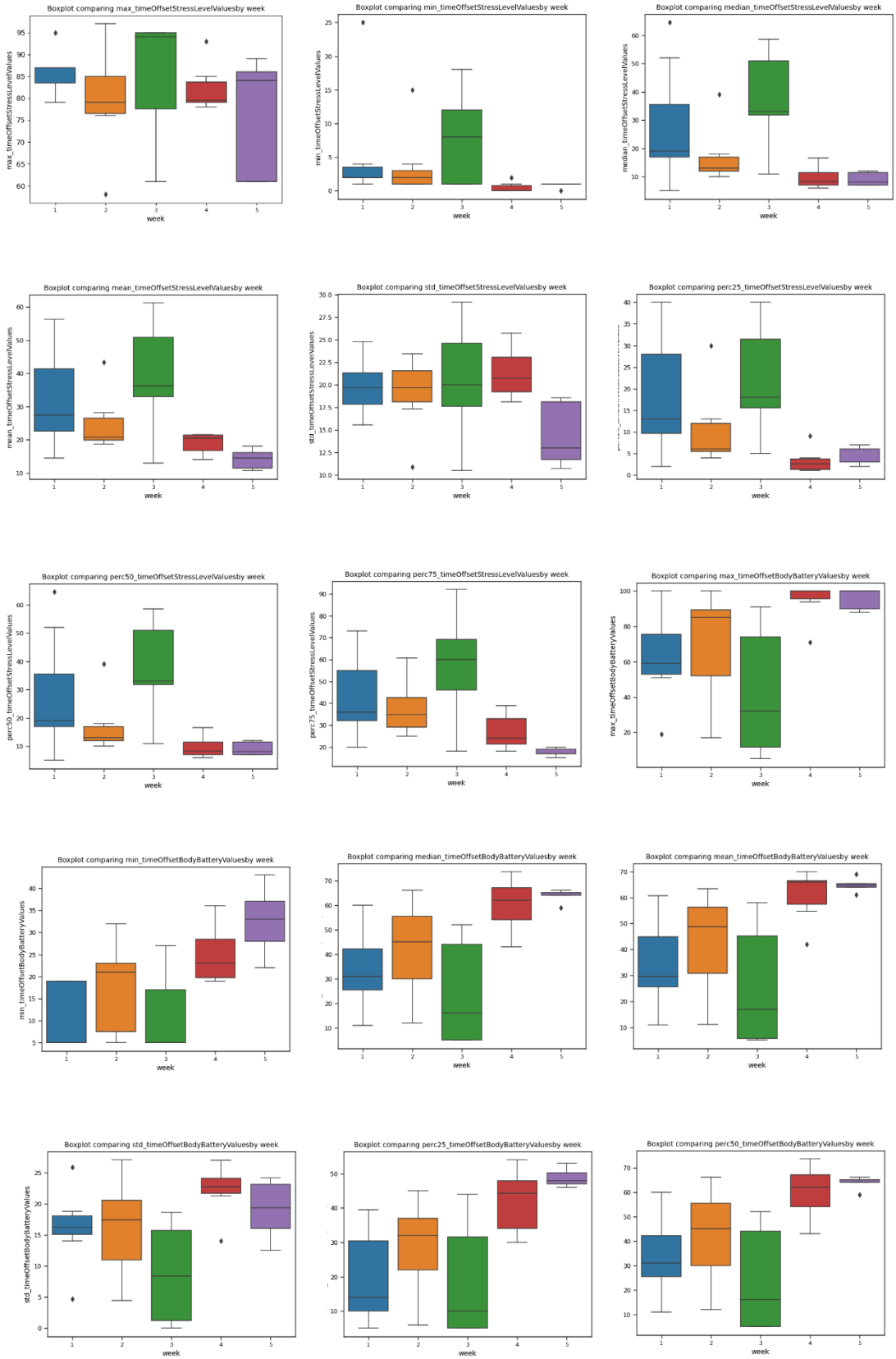


Figure 24 Stress Quantile-quantile plot – Subj 2


Boxplot comparing max_timeOffsetStressLevelValuesby week
max_timeOffsetStressLevelValues
week
Boxplot comparing min_timeOffsetStressLevelValuesby week
min_timeOffsetStressLevelValues
week
Boxplot comparing median_timeOffsetStressLevelValuesby week
median_timeOffsetStressLevelValues
week
Boxplot comparing mean_timeOffsetStressLevelValuesby week
mean_timeOffsetStressLevelValues
week
Boxplot comparing std_timeOffsetStressLevelValuesby week
std_timeOffsetStressLevelValues
week
Boxplot comparing perc25_timeOffsetStressLevelValuesby week
week
Boxplot comparing perc50_timeOffsetStressLevelValuesby week
perc50_timeOffsetStressLevelValues
week
Boxplot comparing perc75_timeOffsetStressLevelValuesby week
perc75_timeOffsetStressLevelValues
week
Boxplot comparing max_timeOffsetBodyBatteryValuesby week
max_timeOffsetBodyBatteryValues
week
Boxplot comparing min_timeOffsetBodyBatteryValuesby week
min_timeOffsetBodyBatteryValues
week
Boxplot comparing median_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing mean_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing std_timeOffsetBodyBatteryValuesby week
std_timeOffsetBodyBatteryValues
week
Boxplot comparing perc25_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing perc50_timeOffsetBodyBatteryValuesby week
week

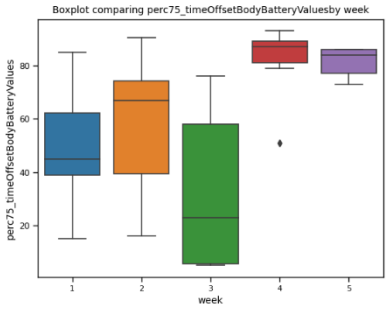
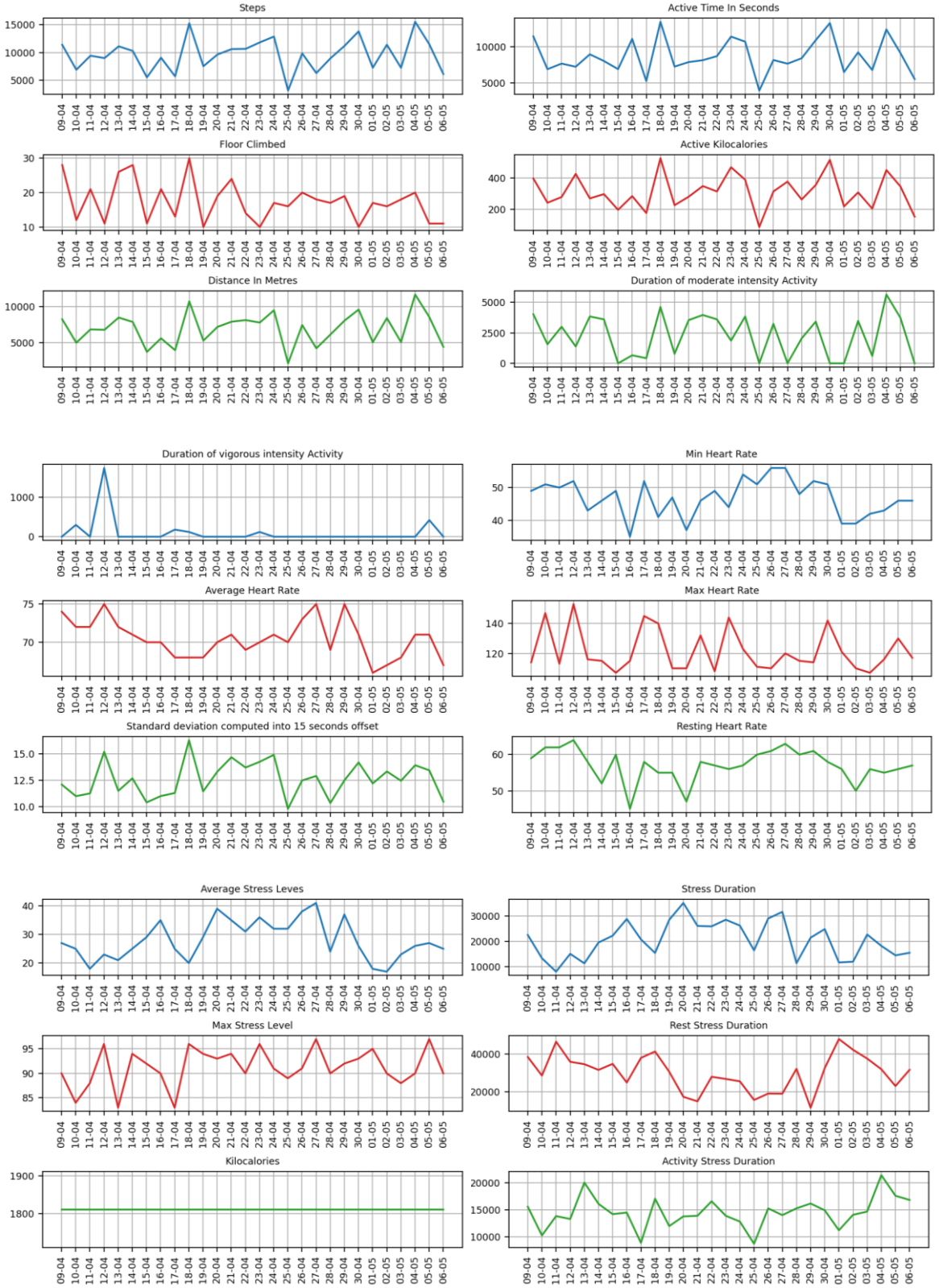


Figure 25 Stress Box plot – Subj 2


Steps
Active Time In Seconds
Floor Climbed
Active Kilocalories
Distance In Metres
Duration of moderate intensity Activity
Duration of vigorous intensity Activity
Min Heart Rate
Average Heart Rate
Max Heart Rate
Standard deviation computed into 15 seconds offset
Resting Heart Rate
Average Stress Leves
Stress Duration
Max Stress Level
Rest Stress Duration
Kilocalories
Activity Stress Duration

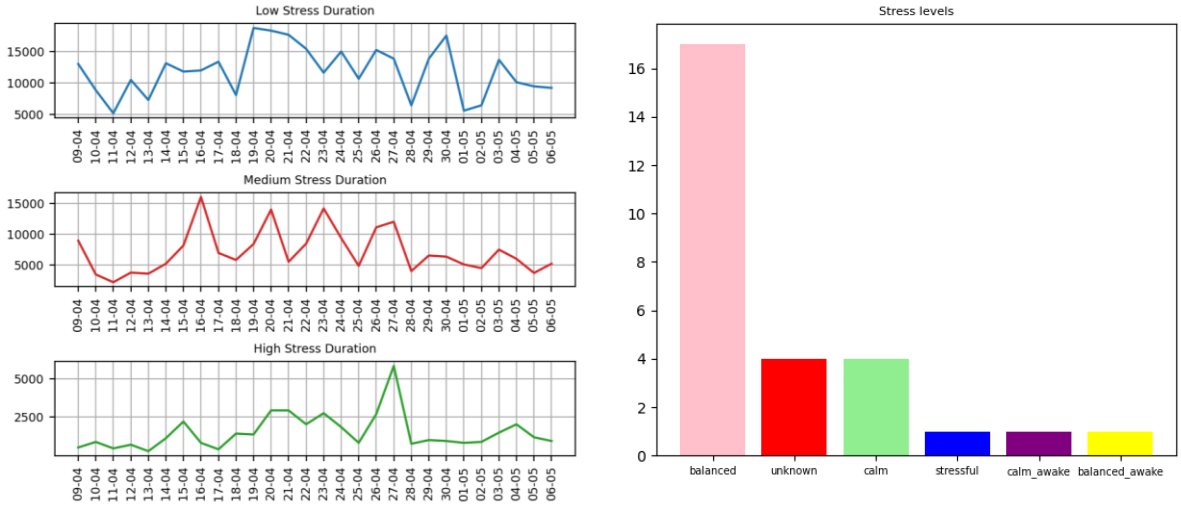


Figure 26 Dailies summaries plot – Subj 3

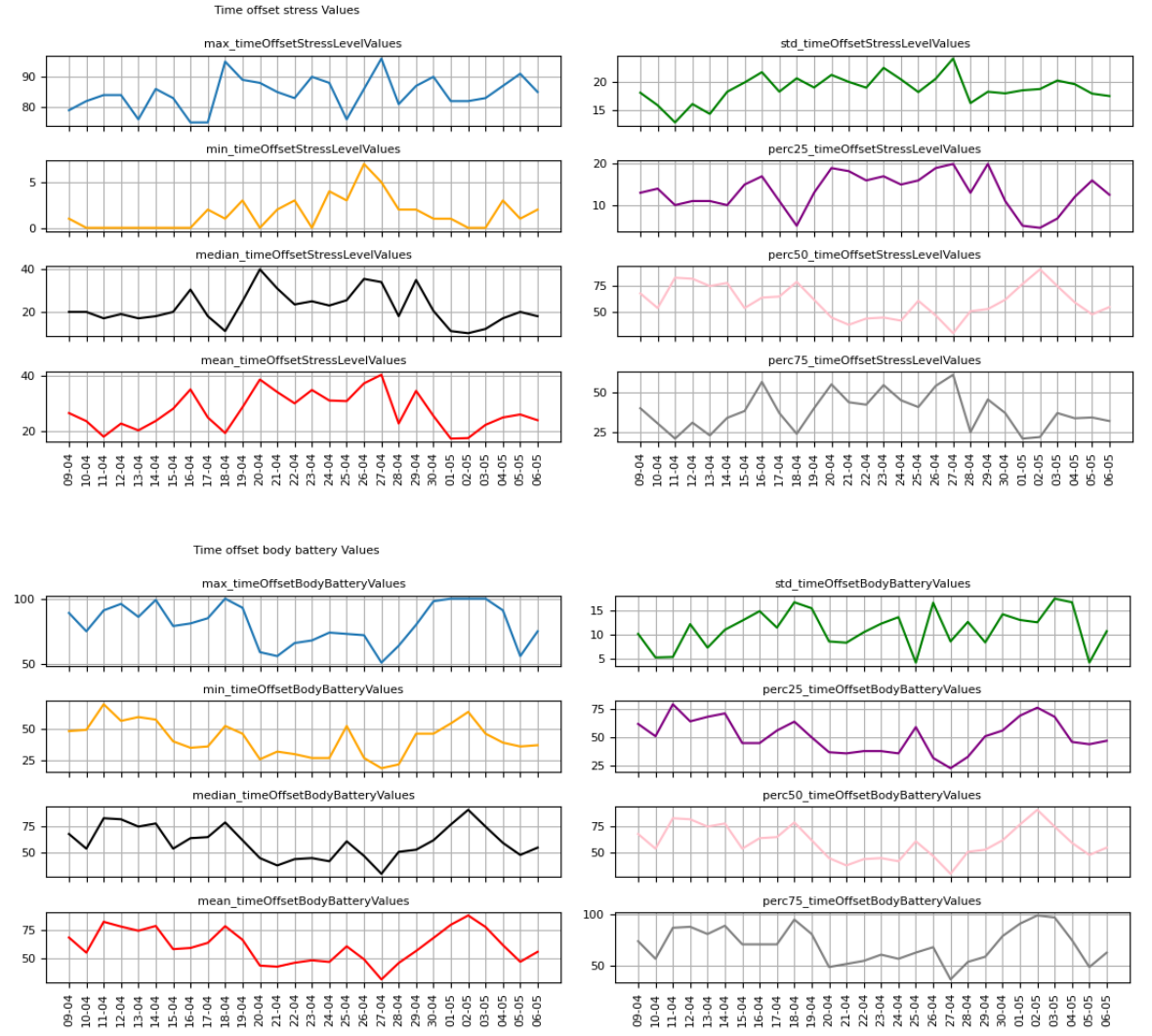


Figure 27 Stress summaries plot – Subj 3

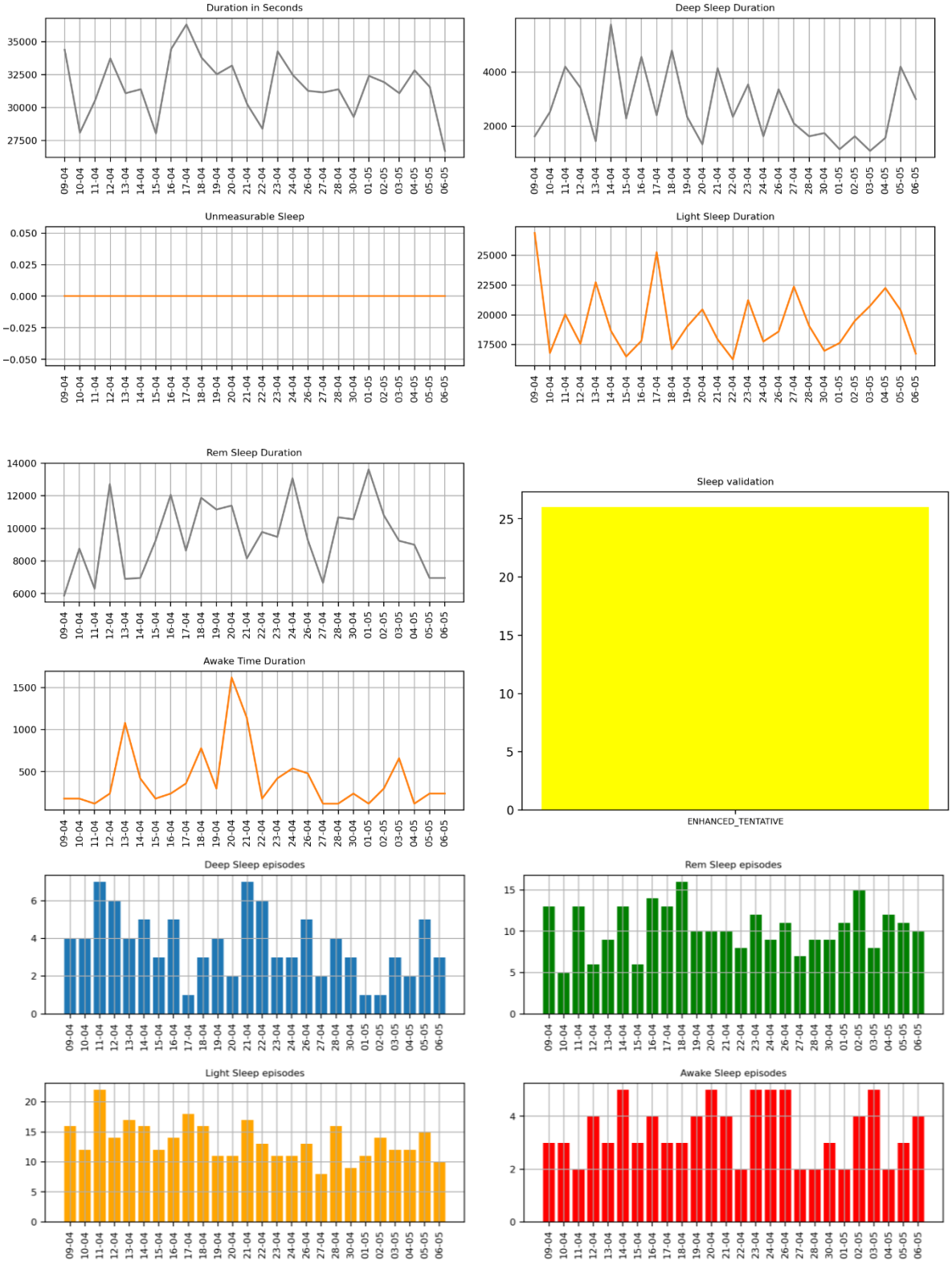


Figure 28 Sleep summary plot – Subj 3

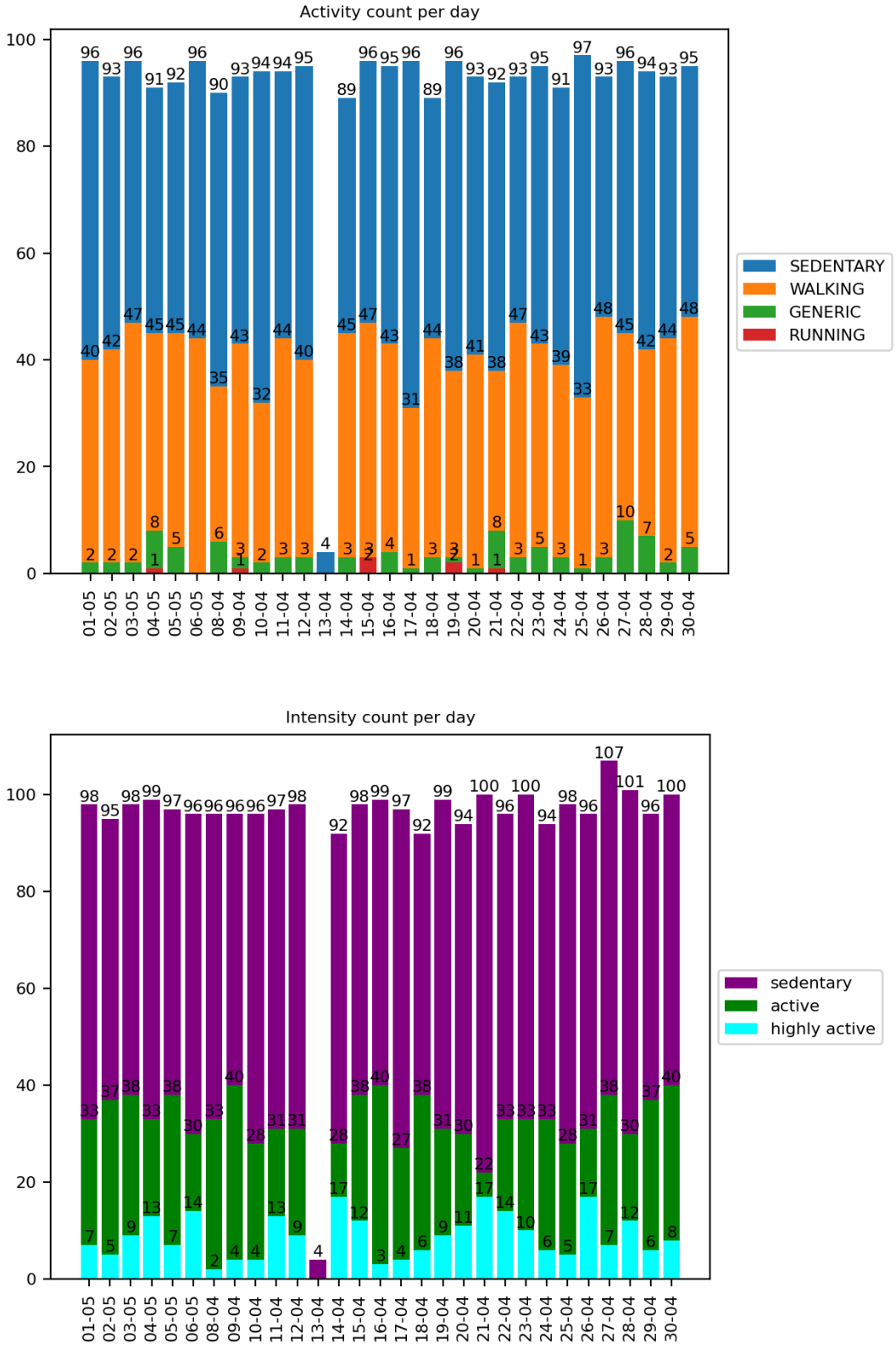
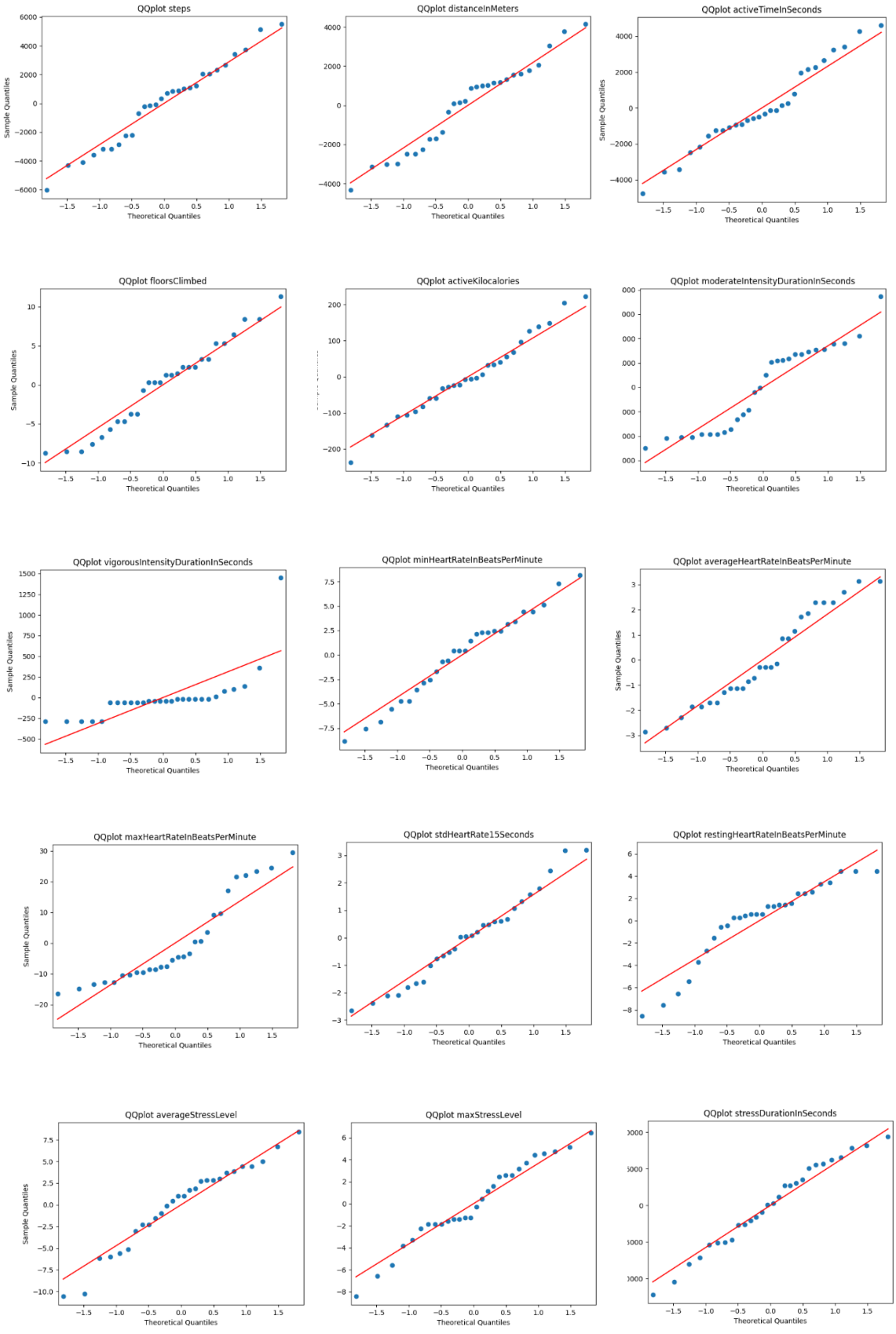


Figure 29 Epochs summaries plot – Subj 3


QQplot steps
QQplot distanceInMeters
QQplot activeTimeInSeconds
QQplot floorsClimbed
QQplot activeKilocalories
QQplot moderateIntensityDurationInSeconds
QQplot vigorousIntensityDurationInSeconds
QQplot minHeartRateInBeatsPerMinute
QQplot averageHeartRateInBeatsPerMinute
QQplot maxHeartRateInBeatsPerMinute
QQplot stdHeartRate15Seconds
QQplot restingHeartRateInBeatsPerMinute
QQplot averageStressLevel
QQplot maxStressLevel
QQplot stressDurationInSeconds
Sample Quantiles
Theoretical Quantiles

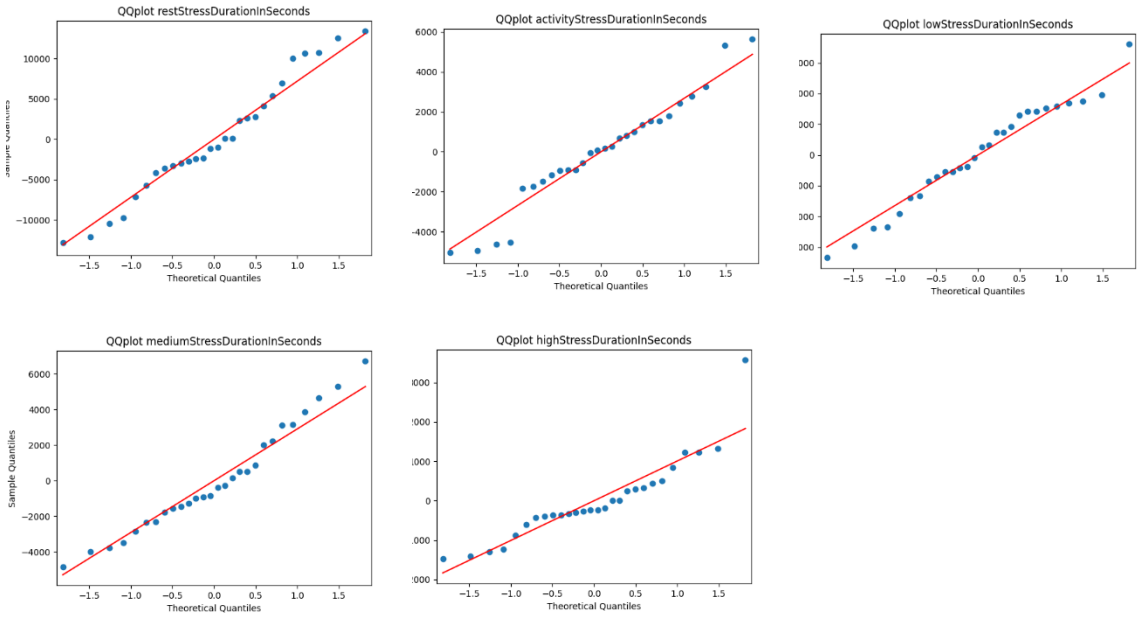
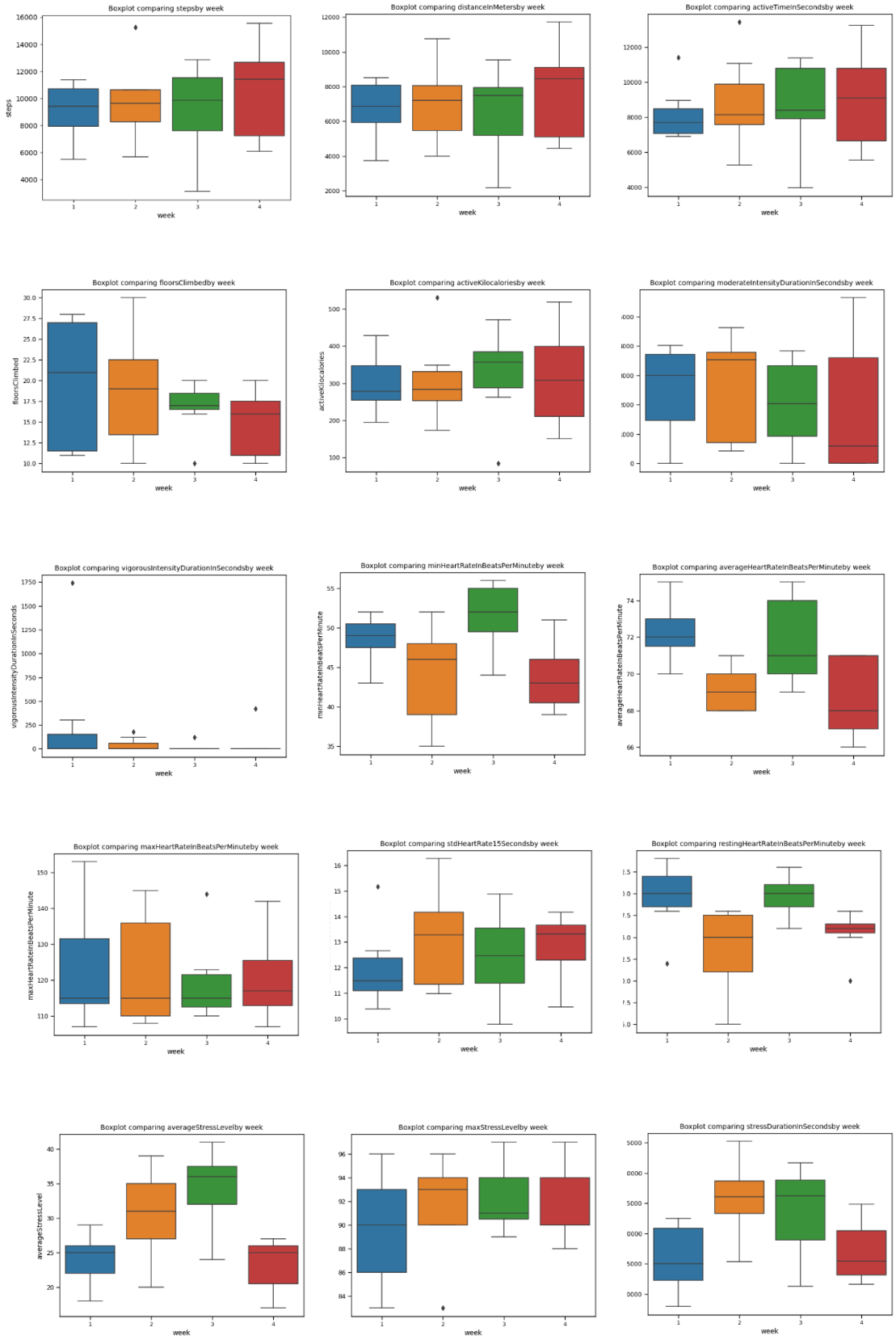


Figure 30 Dailies Quantile-quantile plot – Subj 3


Boxplot comparing stepsby week
steps
week
Boxplot comparing distanceInMetersby week
week
Boxplot comparing activeTimeInSecondsby week
week
Boxplot comparing floorsClimbedby week
floorsClimbed
week
Boxplot comparing activeKilocaloriesby week
activeKilocalories
week
Boxplot comparing moderateIntensityDurationInSecondsby week
week
Boxplot comparing vigorousIntensityDurationInSecondsby week
vigorousIntensityDurationInSeconds
week
Boxplot comparing minHeartRateInBeatsPerMinuteby week
minHeartRateInBeatsPerMinute
week
Boxplot comparing averageHeartRateInBeatsPerMinuteby week
averageHeartRateInBeatsPerMinute
week
Boxplot comparing maxHeartRateInBeatsPerMinuteby week
maxHeartRateInBeatsPerMinute
week
Boxplot comparing stdHeartRate15Secondsby week
week
Boxplot comparing restingHeartRateInBeatsPerMinuteby week
week
Boxplot comparing averageStressLevelby week
averageStressLevel
week
Boxplot comparing maxStressLevelby week
week
Boxplot comparing stressDurationInSecondsby week
week

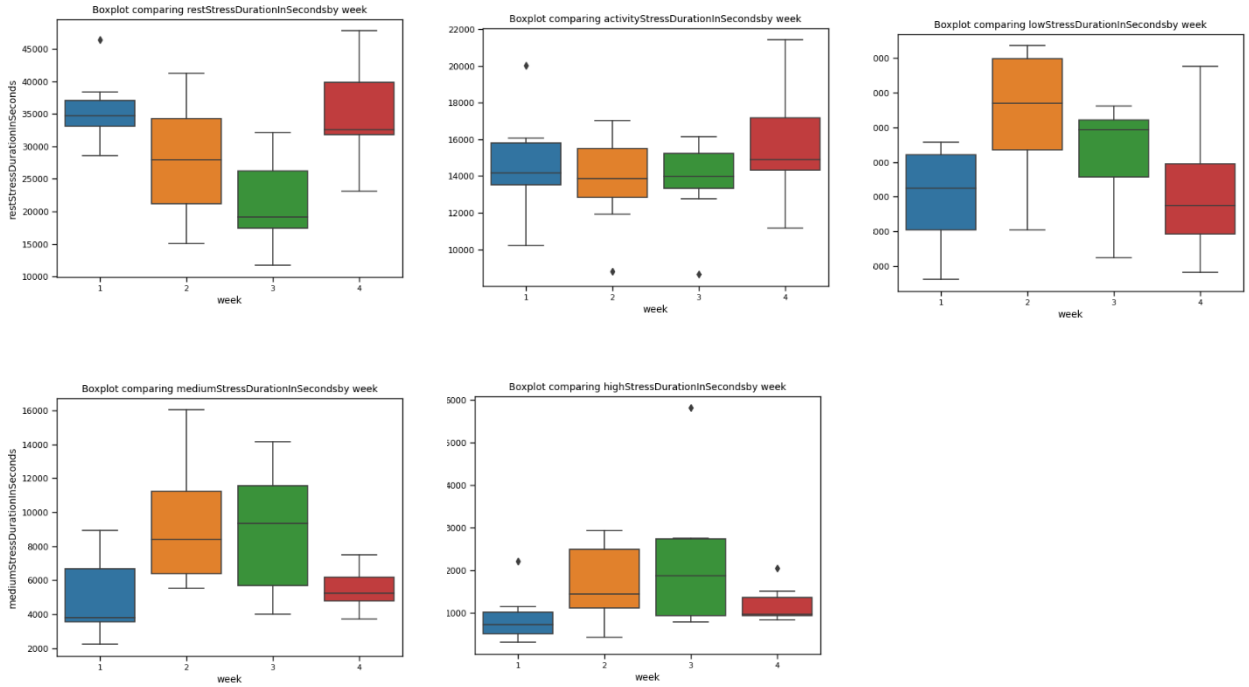


Figure 31 Dailies Box plot - Subj 3

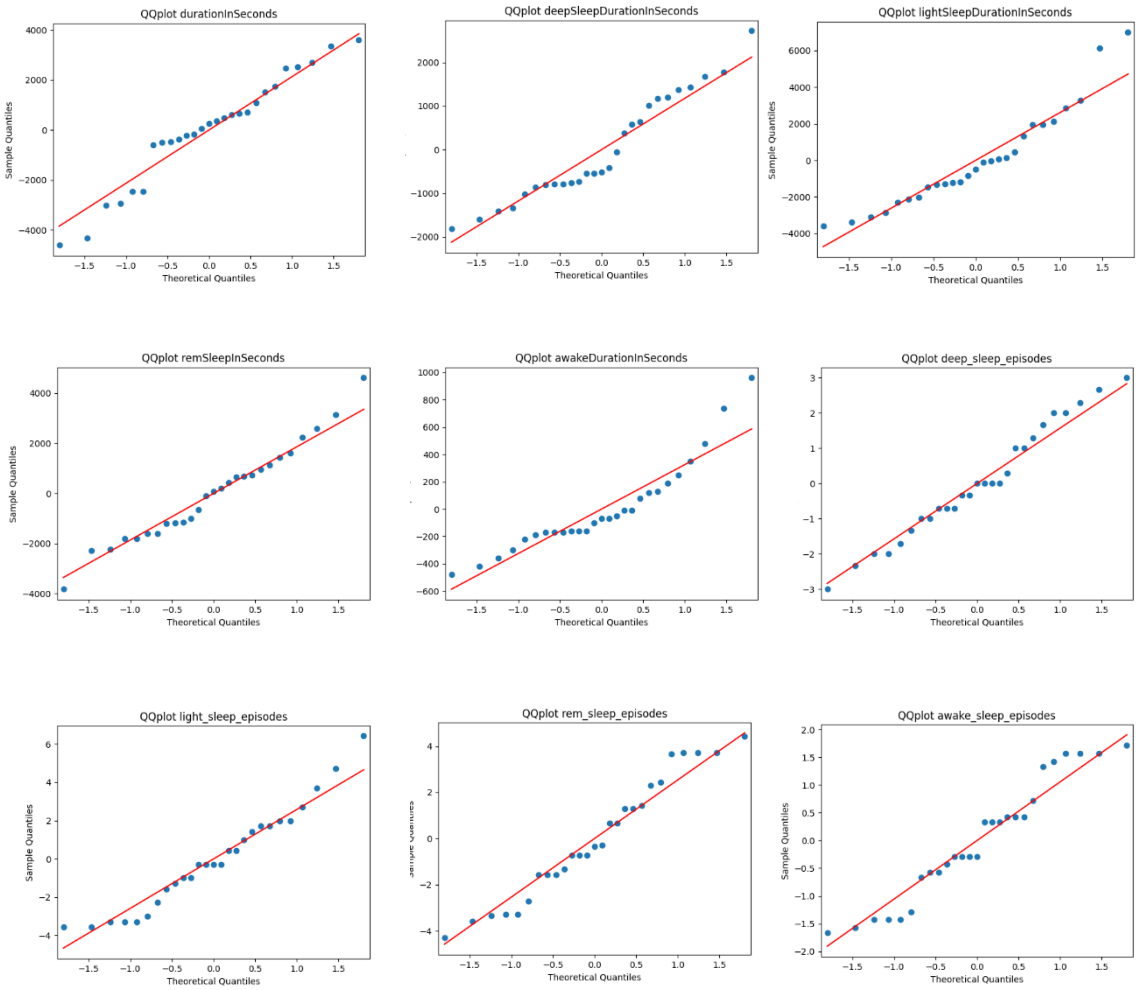


Figure 32 Sleep Quantile-quantile plot – Subj 3

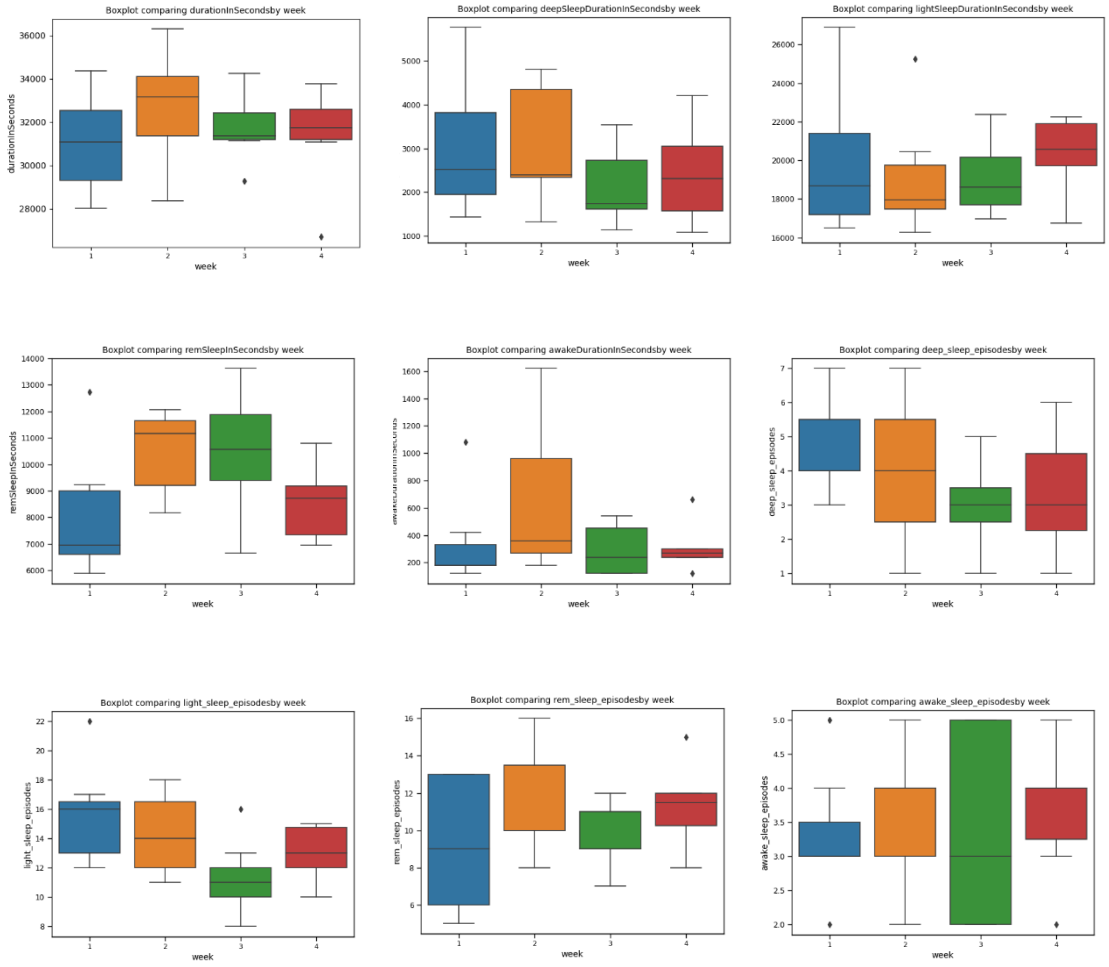
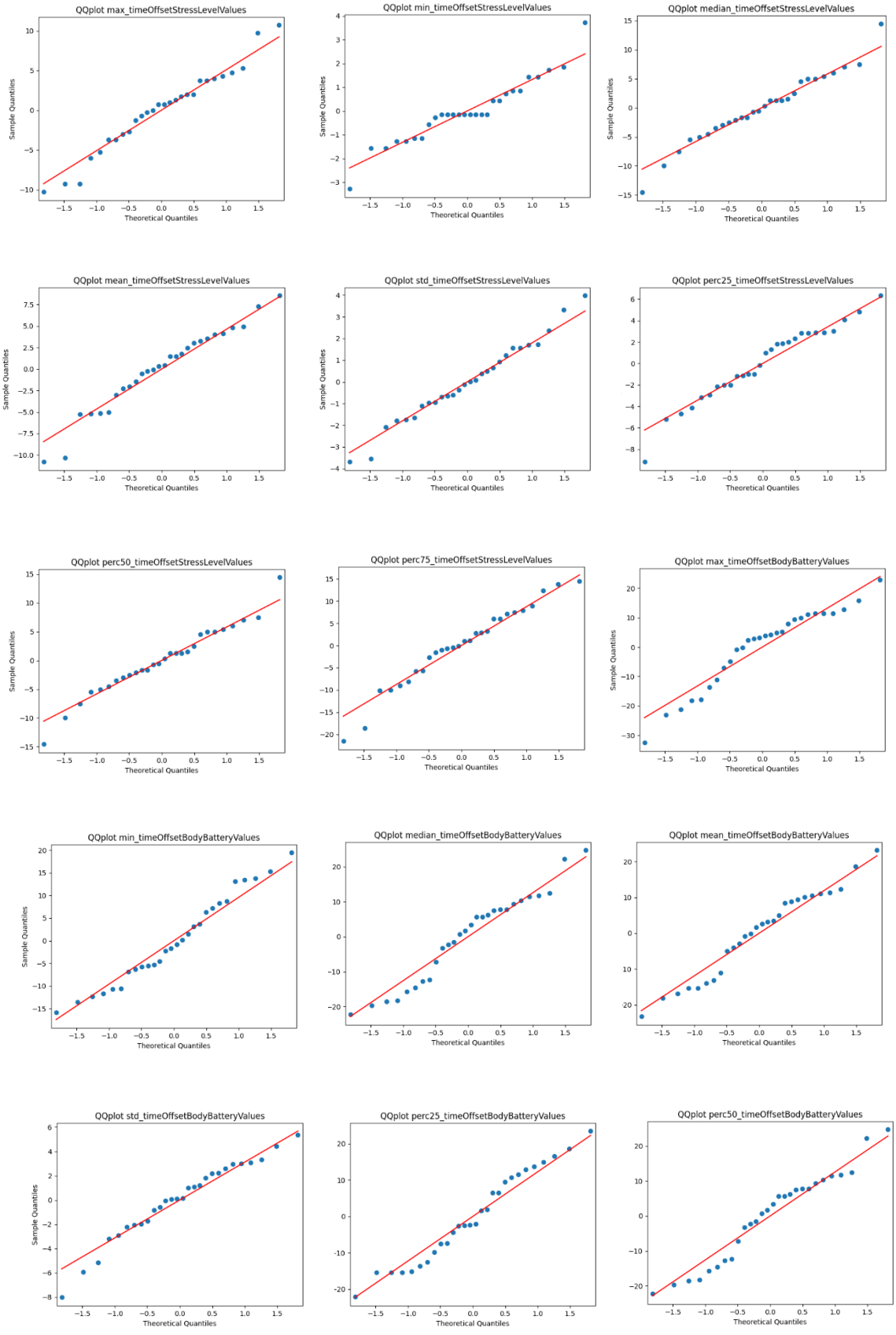


Figure 33 Sleep Box plot – Subj 3


QQplot max_timeOffsetStressLevelValues
QQplot min_timeOffsetStressLevelValues
QQplot median_timeOffsetStressLevelValues
QQplot mean_timeOffsetStressLevelValues
QQplot std_timeOffsetStressLevelValues
QQplot perc25_timeOffsetStressLevelValues
QQplot perc50_timeOffsetStressLevelValues
QQplot perc75_timeOffsetStressLevelValues
QQplot max_timeOffsetBodyBatteryValues
QQplot min_timeOffsetBodyBatteryValues
QQplot median_timeOffsetBodyBatteryValues
QQplot mean_timeOffsetBodyBatteryValues
QQplot std_timeOffsetBodyBatteryValues
QQplot perc25_timeOffsetBodyBatteryValues
QQplot perc50_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles

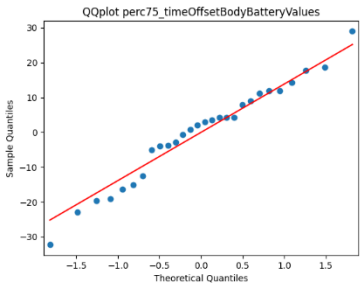
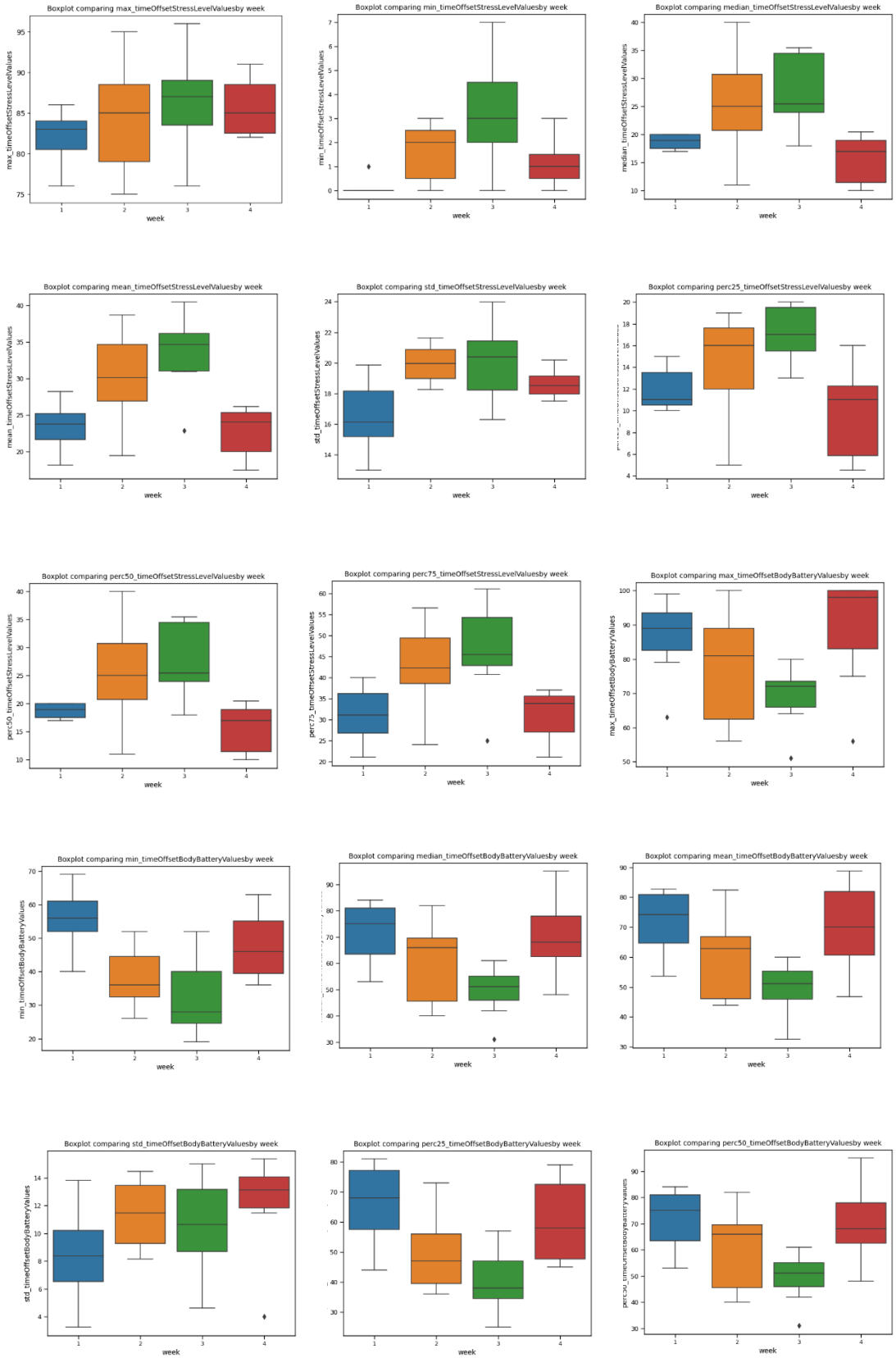


Figure 34 Stress Quantile-quantile plot – Subj 3


Boxplot comparing max_timeOffsetStressLevelValuesby week
max_timeOffsetStressLevelValues
week
Boxplot comparing min_timeOffsetStressLevelValuesby week
min_timeOffsetStressLevelValues
week
Boxplot comparing median_timeOffsetStressLevelValuesby week
median_timeOffsetStressLevelValues
week
Boxplot comparing mean_timeOffsetStressLevelValuesby week
mean_timeOffsetStressLevelValues
week
Boxplot comparing std_timeOffsetStressLevelValuesby week
std_timeOffsetStressLevelValues
week
Boxplot comparing perc25_timeOffsetStressLevelValuesby week
week
Boxplot comparing perc50_timeOffsetStressLevelValuesby week
perc50_timeOffsetStressLevelValues
week
Boxplot comparing perc75_timeOffsetStressLevelValuesby week
perc75_timeOffsetStressLevelValues
week
Boxplot comparing max_timeOffsetBodyBatteryValuesby week
max_timeOffsetBodyBatteryValues
week
Boxplot comparing min_timeOffsetBodyBatteryValuesby week
min_timeOffsetBodyBatteryValues
week
Boxplot comparing median_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing mean_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing std_timeOffsetBodyBatteryValuesby week
std_timeOffsetBodyBatteryValues
week
Boxplot comparing perc25_timeOffsetBodyBatteryValuesby week
week
Boxplot comparing perc50_timeOffsetBodyBatteryValuesby week
week

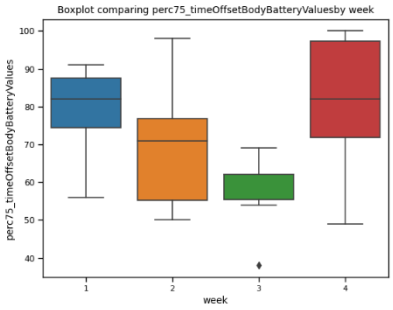
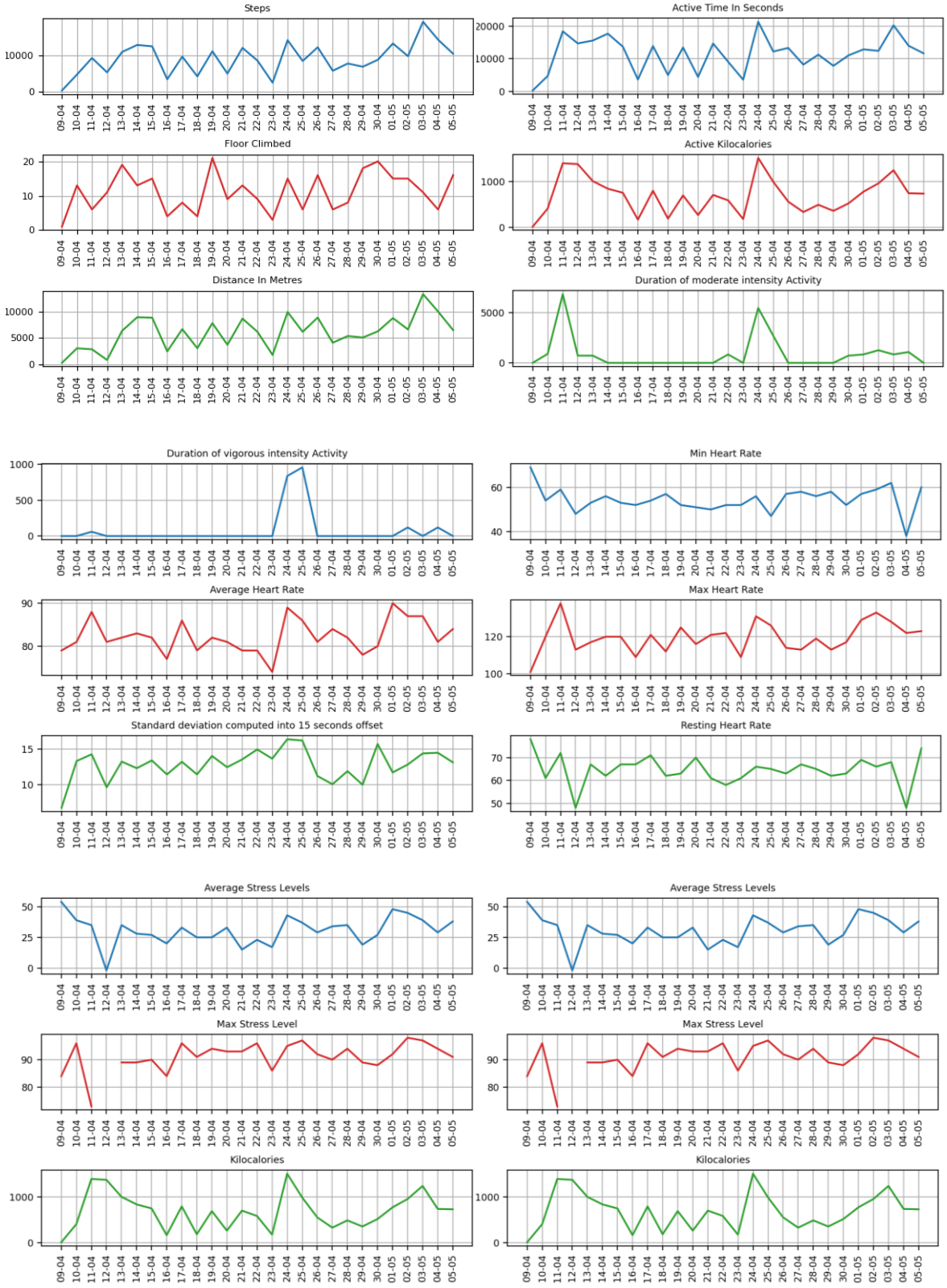


Figure 35 Stress Box plot – Subj 3


Steps
Active Time In Seconds
Floor Climbed
Active Kilocalories
Distance In Metres
Duration of moderate intensity Activity
Duration of vigorous intensity Activity
Min Heart Rate
Average Heart Rate
Max Heart Rate
Standard deviation computed into 15 seconds offset
Resting Heart Rate
Average Stress Levels
Average Stress Levels
Max Stress Level
Max Stress Level
Kilocalories
Kilocalories

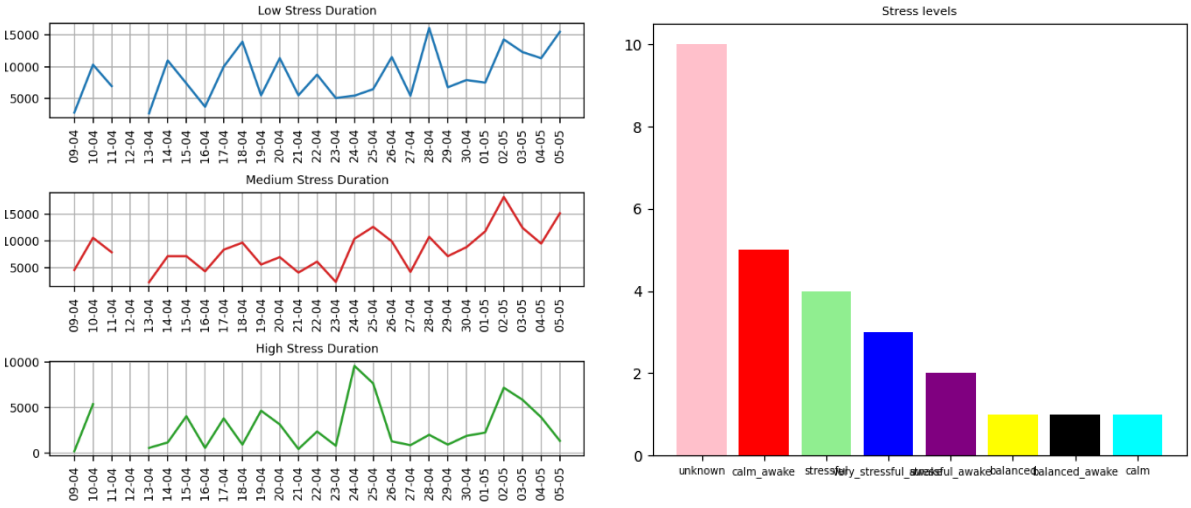


Figure 36. Dailies summaries plot – Subj 4

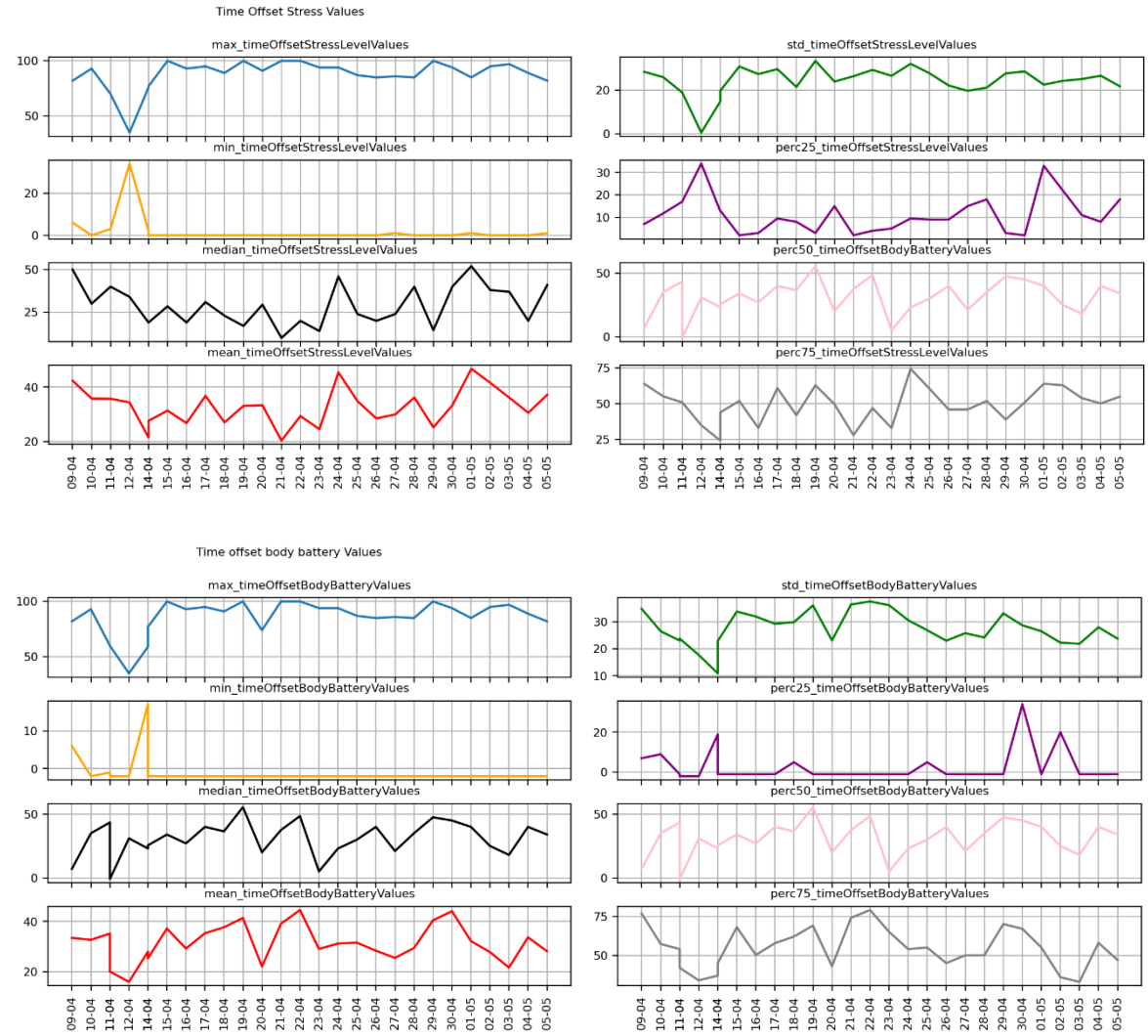


Figure 37. Stress summaries plot – Subj 4

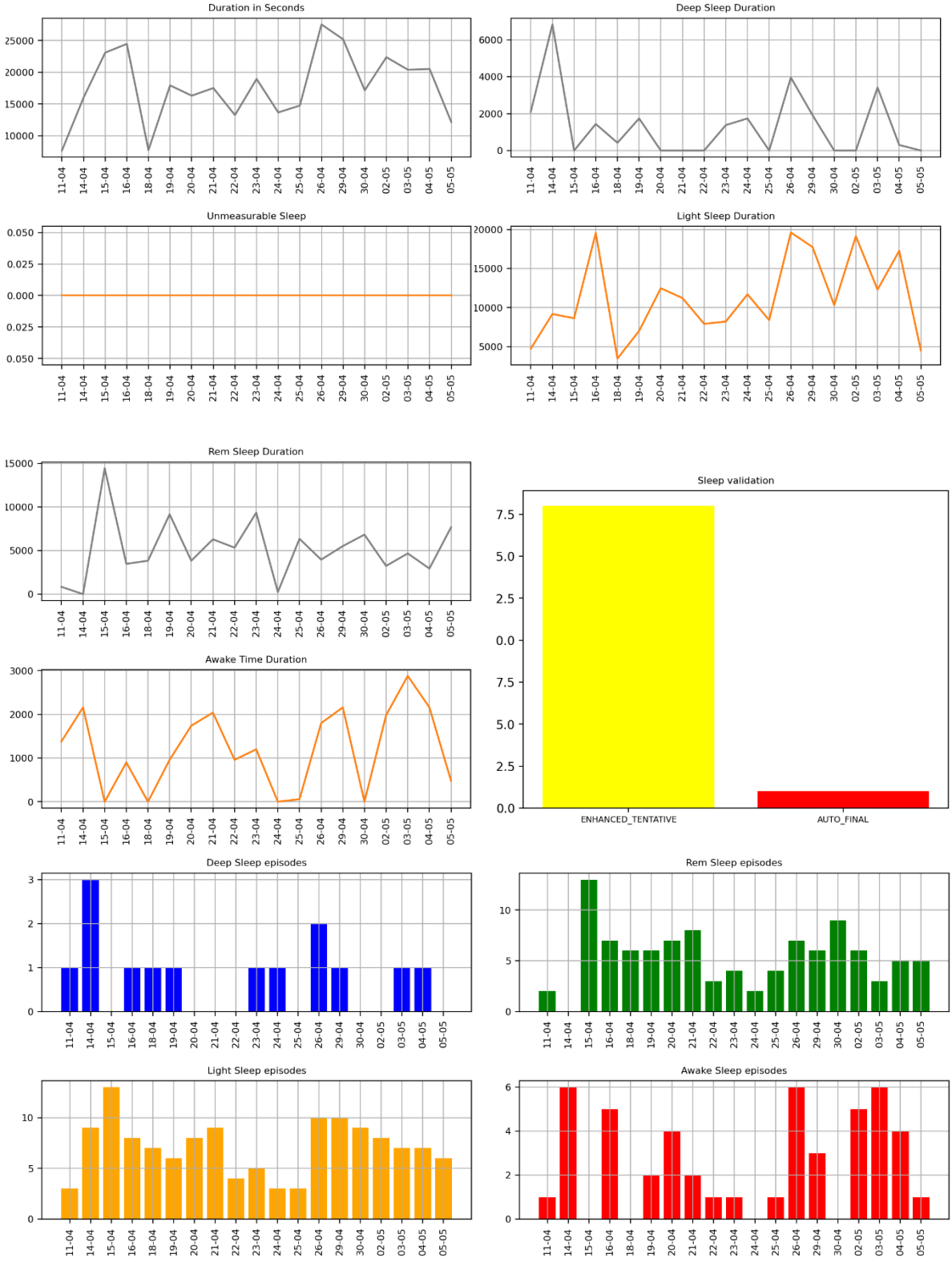


Figure 38. Sleep summary plot – Subj 4

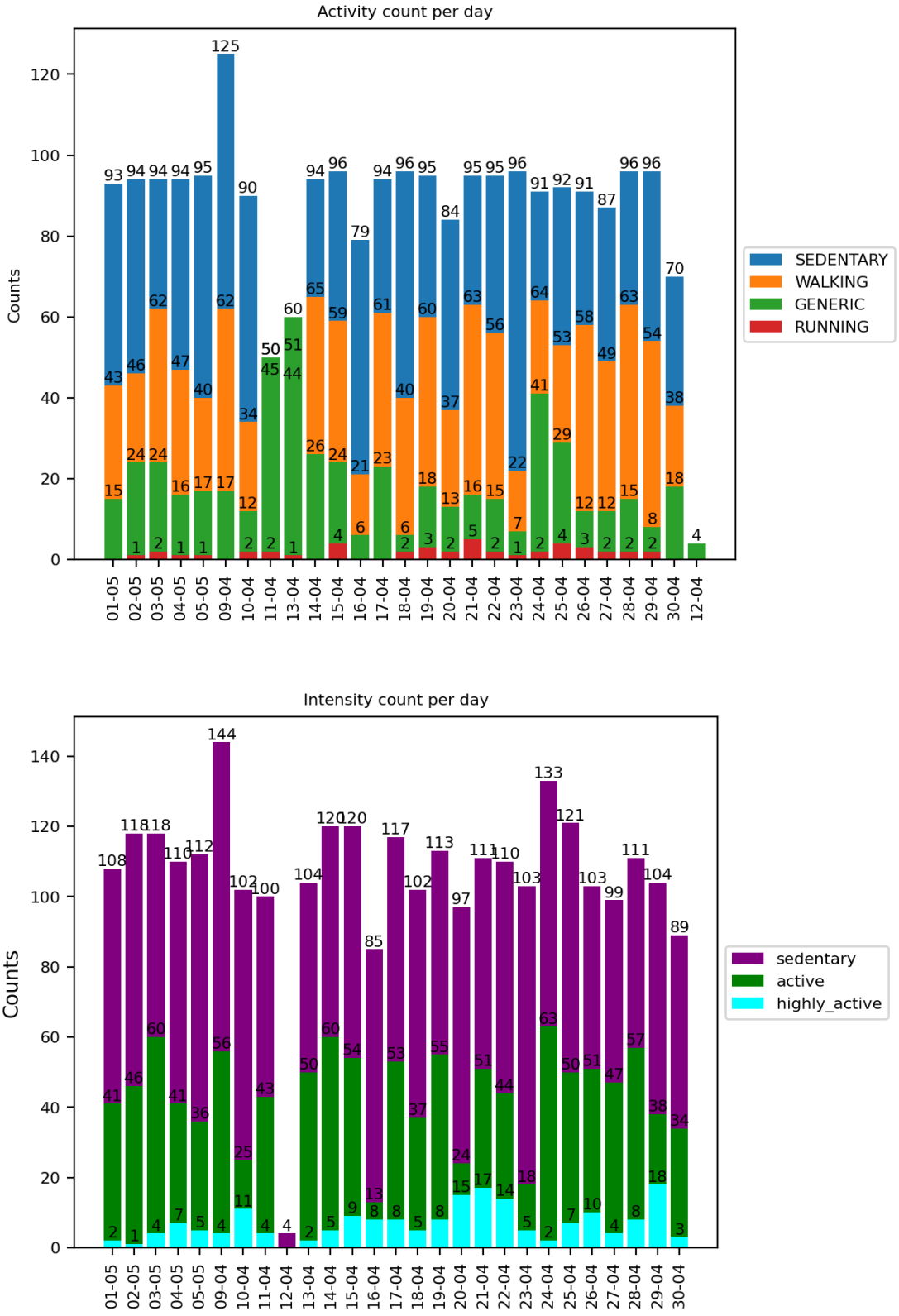
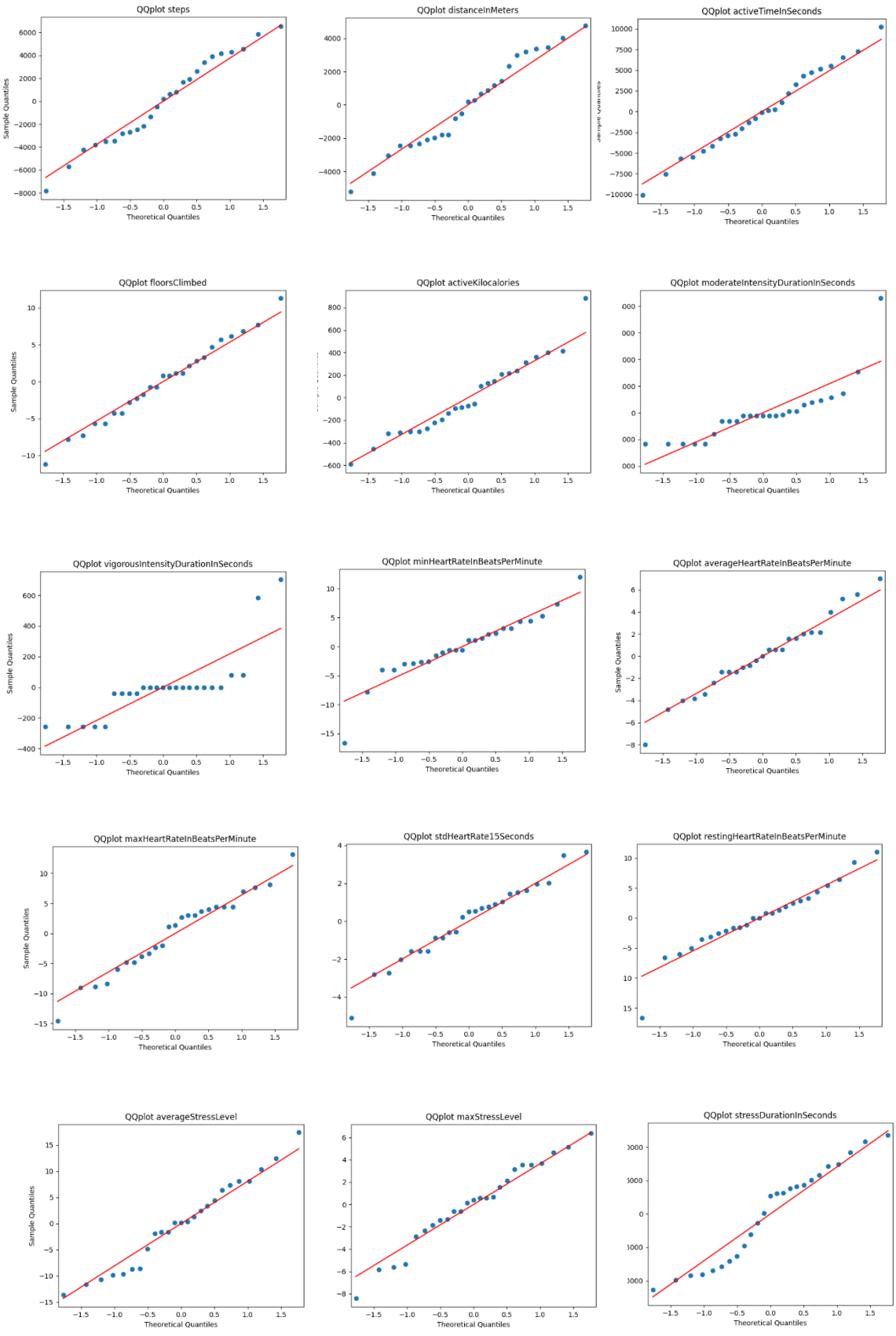


Figure 39. Epochs summaries plot – Subj 4


QQplot steps
QQplot distanceInMeters
QQplot activeTimeInSeconds
QQplot floorsClimbed
QQplot activeKilocalories
QQplot moderateIntensityDurationInSeconds
QQplot vigorousIntensityDurationInSeconds
QQplot minHeartRateInBeatsPerMinute
QQplot averageHeartRateInBeatsPerMinute
QQplot maxHeartRateInBeatsPerMinute
QQplot stdHeartRate15Seconds
QQplot restingHeartRateInBeatsPerMinute
QQplot averageStressLevel
QQplot maxStressLevel
QQplot stressDurationInSeconds
Sample Quantiles
Theoretical Quantiles

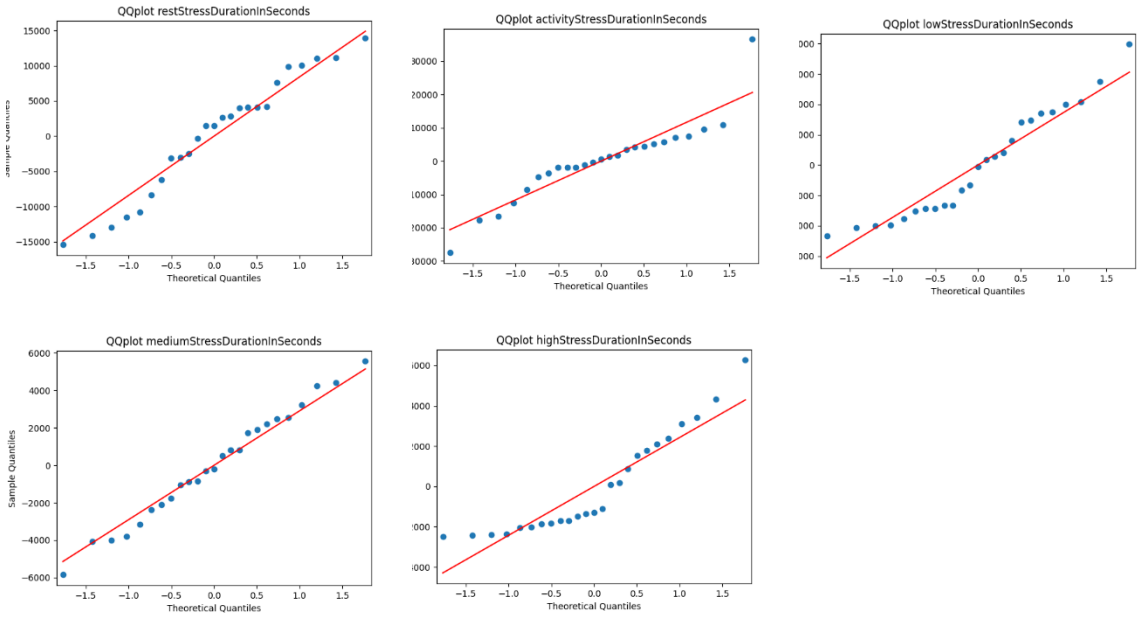
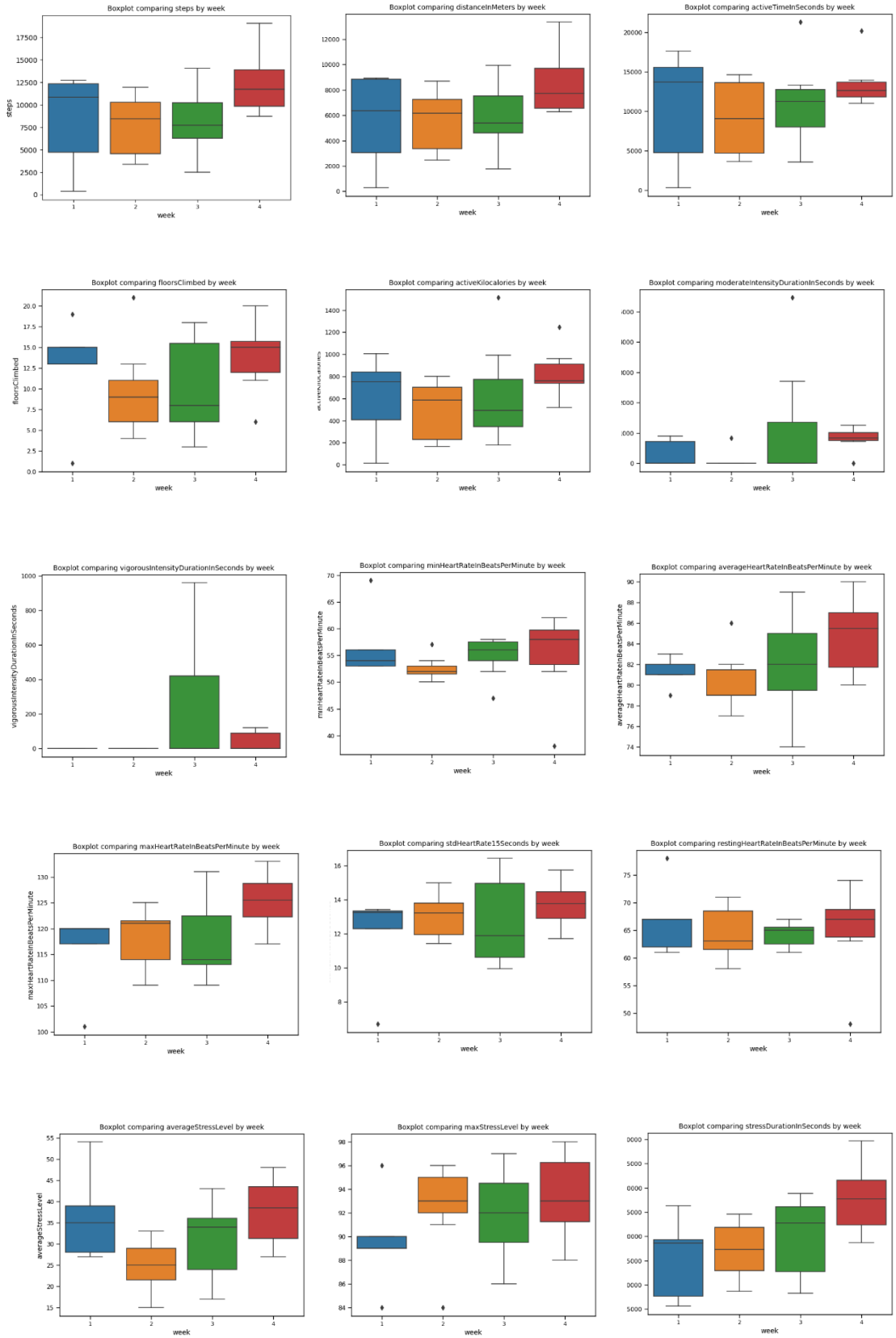


Figure 40. Dailies Quantile-quantile plot – Subj 4


Boxplot comparing steps by week
steps
week
Boxplot comparing distanceInMeters by week
week
Boxplot comparing activeTimeInSeconds by week
week
Boxplot comparing floorsClimbed by week
floorsClimbed
week
Boxplot comparing activeKilocalories by week
week
Boxplot comparing moderateIntensityDurationInSeconds by week
week
Boxplot comparing vigorousIntensityDurationInSeconds by week
vigorousIntensityDurationInSeconds
week
Boxplot comparing minHeartRateInBeatsPerMinute by week
minHeartRateInBeatsPerMinute
week
Boxplot comparing averageHeartRateInBeatsPerMinute by week
averageHeartRateInBeatsPerMinute
week
Boxplot comparing maxHeartRateInBeatsPerMinute by week
maxHeartRateInBeatsPerMinute
week
Boxplot comparing stdHeartRate15Seconds by week
week
Boxplot comparing restingHeartRateInBeatsPerMinute by week
week
Boxplot comparing averageStressLevel by week
averageStressLevel
week
Boxplot comparing maxStressLevel by week
week
Boxplot comparing stressDurationInSeconds by week
week

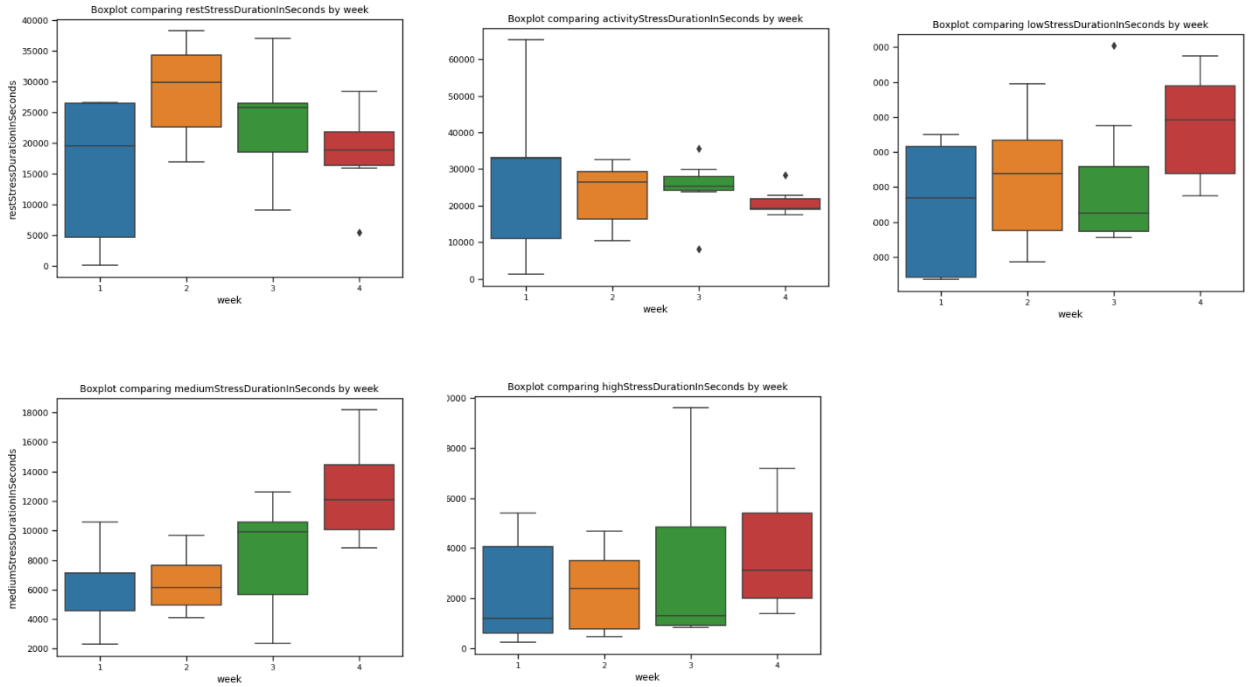


Figure 41. Dailies Box plot - Subj 4

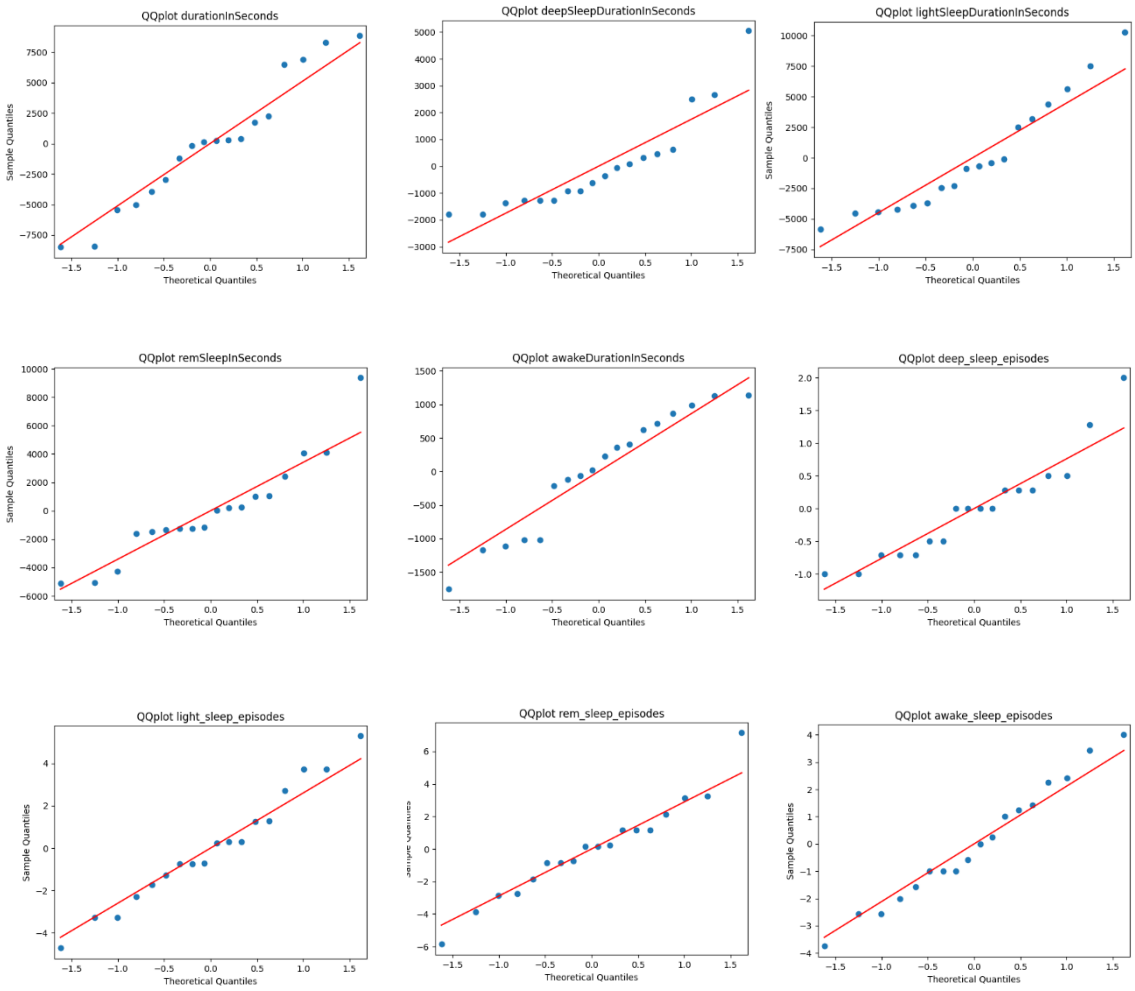


Figure 42. Sleep Quantile-quantile plot – Subj 4

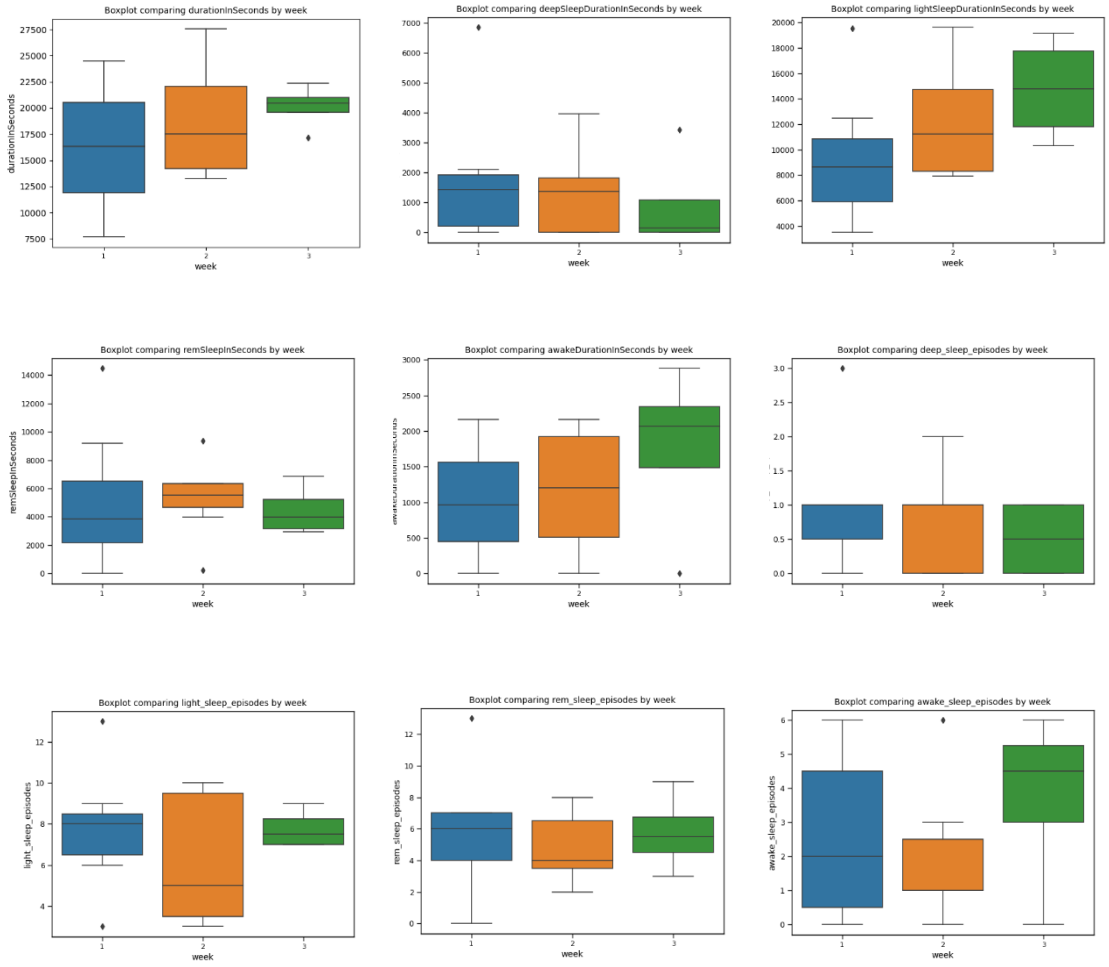
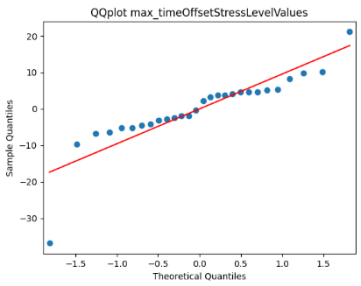
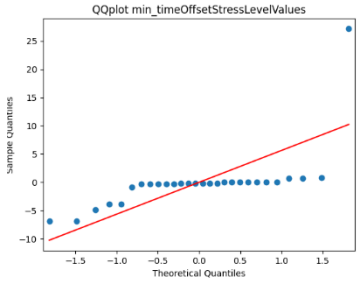
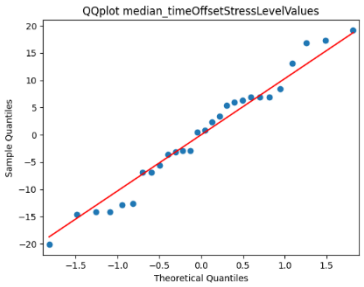
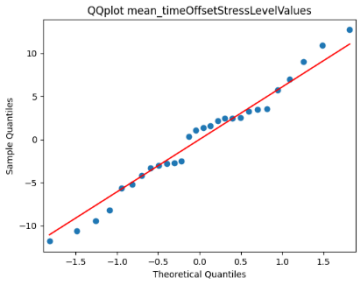


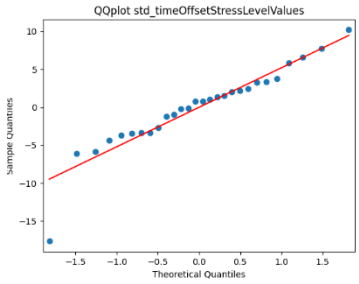
Figure 43. Sleep Boxplot – Subj 4

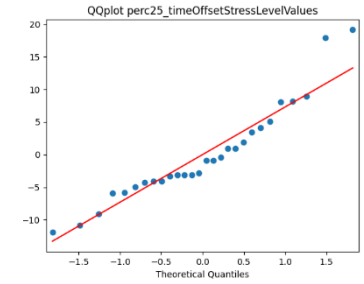

QQplot max_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

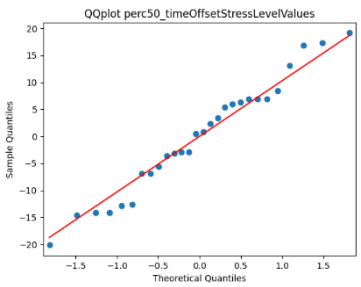

QQplot min_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

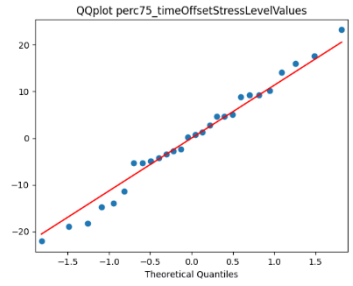

QQplot median_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

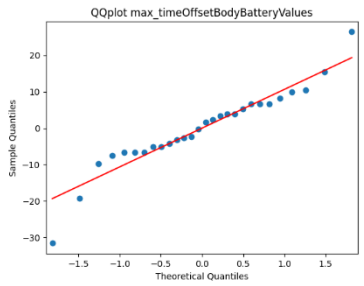

QQplot mean_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

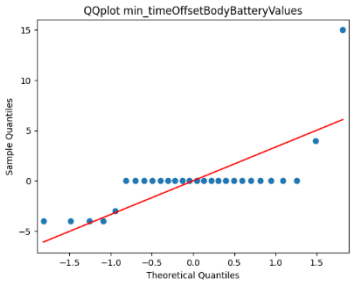

QQplot std_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

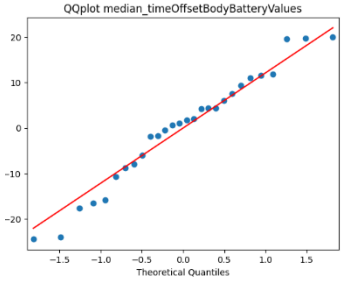

QQplot perc25_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

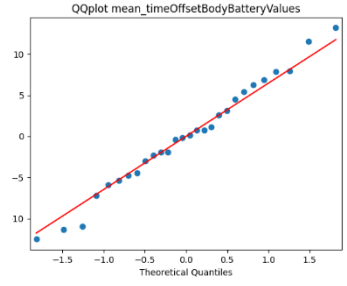

QQplot perc50_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

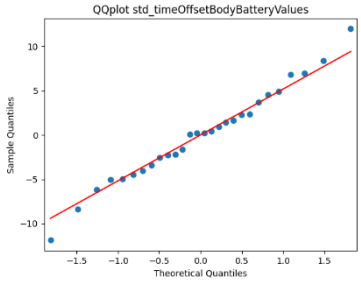

QQplot perc75_timeOffsetStressLevelValues
Sample Quantiles
Theoretical Quantiles

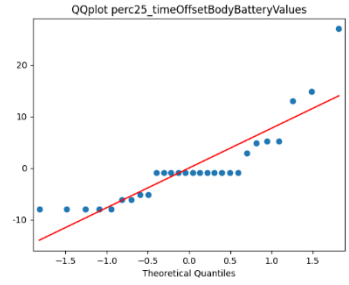

QQplot max_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles

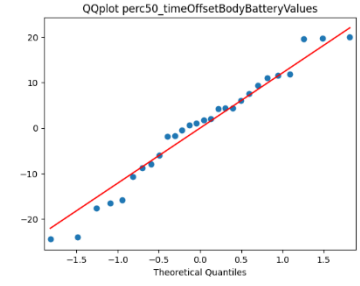

QQplot min_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles


QQplot median_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles


QQplot mean_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles


QQplot std_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles


QQplot perc25_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles


QQplot perc50_timeOffsetBodyBatteryValues
Sample Quantiles
Theoretical Quantiles

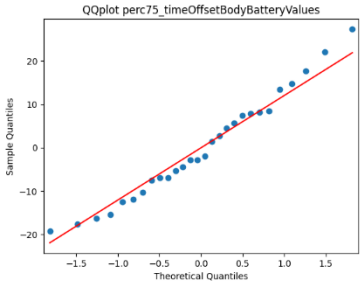
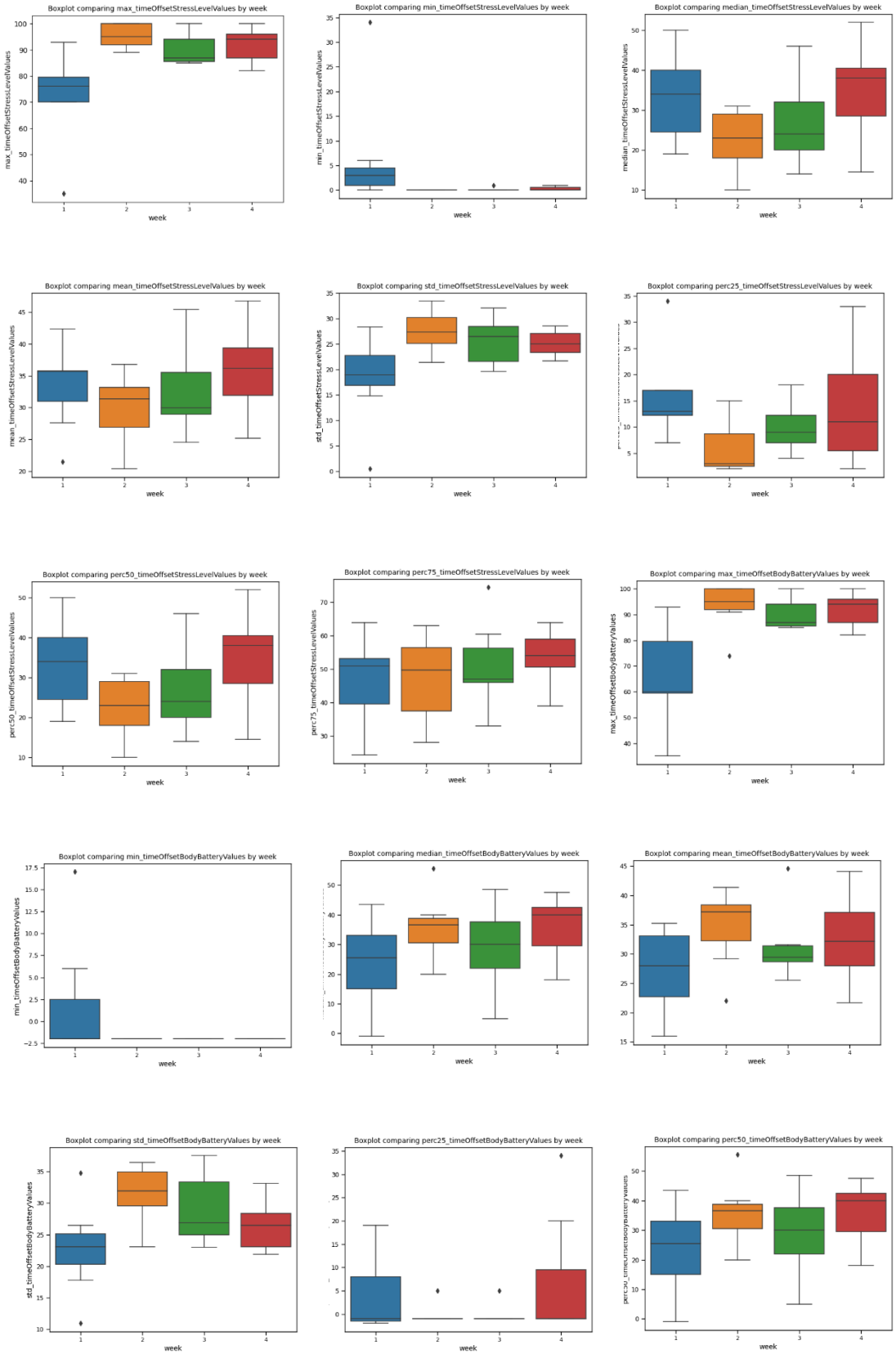


Figure 44. Stress Quantile-quantile plot – Subj 4


Boxplot comparing max_timeOffsetStressLevelValues by week
max_timeOffsetStressLevelValues
week
Boxplot comparing min_timeOffsetStressLevelValues by week
min_timeOffsetStressLevelValues
week
Boxplot comparing median_timeOffsetStressLevelValues by week
median_timeOffsetStressLevelValues
week
Boxplot comparing mean_timeOffsetStressLevelValues by week
mean_timeOffsetStressLevelValues
week
Boxplot comparing std_timeOffsetStressLevelValues by week
std_timeOffsetStressLevelValues
week
Boxplot comparing perc25_timeOffsetStressLevelValues by week
week
Boxplot comparing perc50_timeOffsetStressLevelValues by week
perc50_timeOffsetStressLevelValues
week
Boxplot comparing perc75_timeOffsetStressLevelValues by week
perc75_timeOffsetStressLevelValues
week
Boxplot comparing max_timeOffsetBodyBatteryValues by week
max_timeOffsetBodyBatteryValues
week
Boxplot comparing min_timeOffsetBodyBatteryValues by week
min_timeOffsetBodyBatteryValues
week
Boxplot comparing median_timeOffsetBodyBatteryValues by week
week
Boxplot comparing mean_timeOffsetBodyBatteryValues by week
week
Boxplot comparing std_timeOffsetBodyBatteryValues by week
std_timeOffsetBodyBatteryValues
week
Boxplot comparing perc25_timeOffsetBodyBatteryValues by week
week
Boxplot comparing perc50_timeOffsetBodyBatteryValues by week
week

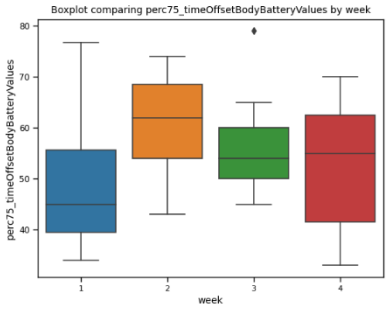


Figure 45. Stress Box plot – Subj 4

TABLES

Table 1. Daily summary

Property	***Type***	***Description***
summaryId	*string*	Unique identifier for the summary.
calendarDate	*string*	The calendar date this summary would be displayed on in Garmin Connect. The date format is 'yyyy-mm-dd.'
startTimeInSeconds	*integer*	Start time of the activity in seconds since January 1, 1970, 00:00:00 UTC (Unix timestamp).
startTimeOffsetInSeconds	*integer*	Offset in seconds to add to startTimeInSeconds to derive the "local" time of the device that captured the data.
activityType	*string*	This field is included in daily summaries for backwards compatibility purposes. It can be ignored and will always default to WALKING.
durationInSeconds	*integer*	Length of the monitoring period in seconds. 86400 once a full day is complete, but less if a user syncs mid-day.
steps	*integer*	Count of steps recorded during the monitoring period.
distanceInMeters	*floating point*	Distance traveled in meters.
activeTimeInSeconds	*integer*	The portion of the monitoring period (in seconds) in which the device wearer was considered Active. This relies on heuristics internal to each device.
activeKilocalories	*integer*	Active kilocalories (dietary calories) burned through actual movement and activity during the monitoring period.

bmrKilocalories	*integer*	BMR Kilocalories burned by existing Basal Metabolic Rate (calculated based on user height/weight/age/other demographic data).
consumedCalories	*integer*	The number of calories that have been consumed by the user through food for that day (value subtracted from calorie goal). This value is received from MyFitnessPal and is not entered within Connect.
moderateIntensityDurationInSeconds	*integer*	Cumulative duration of activities of moderate intensity. Moderate intensity is defined as an activity with MET value range 3-6.
vigorousIntensityDurationInSeconds	*integer*	Cumulative duration of activities of vigorous intensity. Vigorous intensity is defined as activity with MET value > 6.
floorsClimbed	*integer*	Number of floors climbed during the monitoring period.
minHeartRateInBeatsPerMinute	*integer*	Minimum of heart rate values captured during the monitoring period, in beats per minute.
averageHeartRateInBeatsPerMinute	*integer*	Average of heart rate values captured during the last 7 days, in beats per minute. The average heart rate value for the monitoring period can be calculated based on the data from timeOffsetHeartRateSamples.
maxHeartRateInBeatsPerMinute	*integer*	Maximum of heart rate values captured during the monitoring period, in beats per minute.

restingHeartRateInBeatsPerMinute	*Integer*	Average heart rate at rest during the monitoring period, in beats per minute.
timeOffsetHeartRateSamples	*Map*	Collection of mappings between offset from start time (in seconds) to a heart rate value recorded for that time, in beats per minute. Each entry is a representative sample of the previous 15 seconds from the given offset. Lack of entry for a given offset should be interpreted as no data available. For example, in the response below, the user had 75 BPM for the first 30 seconds of the daily summary, took off their device until the 3180 second time slice, and took it off again after the 3255 second entry.
erageStressLevel	*integer*	An abstraction of the user's average stress level in this monitoring period, measured from 1 to 100, or -1 if there is not enough data to calculate average stress. Scores between 1 and 25 are considered "rest" (i.e., not stressful), 26-50 as "low" stress, 51-75 "medium" stress, and 76-100 as "high" stress.
maxStressLevel	*integer*	The highest stress level measurement taken during this monitoring period.
stressDurationInSeconds	*integer*	The number of seconds in this monitoring period where stress level measurements were in the stressful range (26-100).

restStressDurationInSeconds	*integer*	The number of seconds in this monitoring period where stress level measurements were in the restful range (1 to 25).
activityStressDurationInSeconds	*integer*	The number of seconds in this monitoring period where the user was engaging in physical activity and so stress measurement was unreliable. All duration in this monitoring period not covered by stress, rest, and activity stress should be considered Uncategorized, either because the device was not worn or because not enough data could be taken to generate a stress score.
lowStressDurationInSeconds	*integer*	The portion of the user's stress duration where the measured stress score was in the low range (26-50).
mediumStressDurationInSeconds	*integer*	The portion of the user's stress duration where the measured stress score was in the medium range (51-75).
highStressDurationInSeconds	*integer*	The portion of the user's stress duration where the measured stress score was in the high range (76-100).
stressQualifier	*string*	A qualitative label applied based on all stress measurements in this monitoring period. Values: unknown, calm, balanced, stressful, very_stressful, calm_awake, balanced_awake, stressful_awake, very_stressful_awake. This matches what the user will see in

		Garmin Connect. It is recommended that implementations that use the stressQualifier be tolerant of unknown values in case more granular values are added.
stepsGoal	*integer*	The user's step goal for this monitoring period.
netKilocaloriesGoal	*integer*	The user's goal for net caloric intake (consumed calories minus active calories) for this monitoring period. This field is related to integration with MyFitnessPal and may not be present for many users.
intensityDurationGoalInSeconds	*integer*	The user's goal for consecutive seconds of moderate to vigorous intensity activity for this monitoring period.
floorsClimbedGoal	*integer*	The user's goal for floors climbed in this monitoring period.

Table 2. Epochs summary

Property	**Type**	***Description***
summaryId	string	Unique identifier for the summary.
startTimeInSeconds	integer	Start time of the monitoring period in seconds since January 1, 1970, 00:00:00 UTC (Unix timestamp).
startTimeOffsetInSeconds	integer	Offset in seconds to add to startTimeInSeconds to derive the "local" time of the device that captured the data
activityType	string	Text description of the activity type.
durationInSeconds	integer	Length of the monitoring period in seconds.

activeTimeInSeconds	integer	Portion of the monitoring period (in seconds) in which the device wearer was active for this activity type. The sum of active times of all epochs of the same start time (and different activity types) should be equal to the duration.
Steps	integer	Count of steps recorded during the monitoring period
distanceInMeters	floating point	Distance traveled in meters
activeKilocalories	integer	Active kilocalories (dietary calories) burned during the monitoring period. This includes only the calories burned by the activity and not calories burned as part of the basal metabolic rate (BMR).
Met	floating point	MET (Metabolic Equivalent of Task) value for the active time for this activity type.
intensity	string	Qualitative measure of intensity.
meanMotionIntensity	floating point	The average of motion intensity scores for all minutes in this monitoring period.
maxMotionIntensity	floating point	The largest motion intensity score of any minute in this monitoring period.

Table 3. Stress summary

Property	***Type***	***Description***
summaryId	*string*	Unique identifier for the summary.
startTimeInSeconds	integer	Start time of the summary in seconds since January 1, 1970, 00:00:00 UTC (Unix timestamp).
startTimeOffsetInSeconds	integer	Offset in seconds to add to startTimeInSeconds to derive the

		“local” time of the device that captured the data.
durationInSeconds	integer	The duration of the measurement period in seconds.
calendarDate	string	The calendar date this summary would be displayed on in Garmin Connect. The date format is ‘yyyy-mm-dd.’

Table 4. Sleep summary

Property	***Type***	***Description***
summaryId	*string*	Unique identifier for the summary.
calendarDate	*string*	The calendar date this summary would be displayed on in Garmin Connect. The date format is ‘yyyy-mm-dd.’
startTimeInSeconds	*integer*	Start time of the activity in seconds since January 1, 1970, 00:00:00 UTC (Unix timestamp).
startTimeOffsetInSeconds	*integer*	Offset in seconds to add to startTimeInSeconds to derive the “local” time of the device that captured the data.
durationInSeconds	*integer*	Length of the monitoring period in seconds.
unmeasurableSleepInSeconds	*Integer*	Time in seconds that the sleep level of the user could not be measured. This may or may not correspond to off-wrist time.
deepSleepDurationInSeconds	*integer*	Time in seconds the user spent in deep sleep during the sleep period.
lightSleepDurationInSeconds	*integer*	Time in seconds the user spent in light sleep during the sleep period.

remSleepInSeconds	*integer*	Time in seconds the user spent in REM sleep during the sleep period.
awakeDurationInSeconds	*integer*	Time in seconds the user spent awake during the sleep period.
sleepLevelsMap	*Map*	A map of sleep level time ranges, currently deep, light, and awake. Time ranges are represented as unix timestamps in seconds.
Validation	*string*	sleep start and stop. OFF_WRIST: Device did not have enough heart rate data to make calculations for sleep levels Map. (device was off or too loose). Only start and end sleep times will be provided. AUTO_TENTATIVE: The sleep start and stop times were auto detected by Garmin Connect using accelerometer data. However, it is possible that further refinements to this sleep record will come later. This could be because the user is still asleep or could be because the user owns multiple devices and might synchronize another device later for this same period. AUTO_FINAL: The sleep start and stop times were auto detected by Garmin Connect, and enough data has been gathered to finalize the window. This status also indicates that the user only has one device so this record can never be updated again – users that own

		multiple devices will never get an AUTO_FINAL. AUTO_MANUAL: Sleep data was auto-detected by Garmin Connect, but the user is overriding the start and stop times, or the user started with a manual entry and the sleep was auto-detected later. Garmin Connect stores both but will display the manual start and stop times in favor of the auto-detected times. ENHANCED_TENTATIVE: Sleep data was collected from a device capable of running an enhanced sleep analysis to detect REM sleep, but an updated sleep summary record may come later with further refinements or a greater sleep period. ENHANCED_FINAL: Sleep data was collected from a device capable of running an enhanced sleep analysis to detect REM sleep, and no further updates or refinements to this sleep analysis are expected.
timeOffsetSleepRespiration	*Map*	Collection of key-value pairs where the key is offset in seconds from the startTimeInSeconds, and respiration measurement taken at that time. Respiration measurement is in breaths per minute.

timeOffsetSleepSpo2	*Map*	A map of SpO2 readings, where the keys are the offsets in seconds from the startTimeInSeconds and the values are the SpO2 measurements at that time. Only present if the user's device is SpO2-enabled.
overallSleepScore	*Map*	A map of overall sleep score, containing the quantitative value and the qualitative description of sleep.
sleepScores	*Map*	A map of sleep score string descriptions for each type of sleep as well as restless periods and stress levels during sleep. Each entry in the sleepScores will have a qualifierKey value of EXCELLENT, GOOD, FAIR, or POOR that is used as a qualitative description of the user's period of sleep.

Table 5. Percentage of completion and time of participation in the rehabilitation program per patient

PARTICIPANT	***% OF TRAINING***	***TIME OF TRAINING***
First	25%	2h 13m
Second	8%	5m
Third	44%	7h 16 m
Fourth	14%	1h 10m
Fifth	0%	0

Table 6. ANOVA test assumption results for dailies summaries - Subj 1

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
steps	0,68	0,29
distanceinmeters	0,63	0,33
activetimeinseconds	0,66	0,51
floorsclimbed	**<0,001**	0,90
activekilocalories	**0,02**	0,44
moderateintensitydurationinseconds	**<0.001**	0,42
vigorousintensitydurationinseconds	**<0.001**	0,42
minheartrateinbeatsperminute	0,20	0,32
averageheartrateinbeatsperminute	0,60	0,99
maxheartrateinbeatsperminute	**0,005**	0,75
stdheartrate15seconds	**0,19**	0,32
restingheartrateinbeatsperminute	**0,02**	0,91
averagestresslevel	**0,03**	0,86
maxstresslevel	0,29	0,54
stressdurationinseconds	**0,002**	0,70
reststressdurationinseconds	0,37	0,89
activitystressdurationinseconds	0.5	0,96
lowstressdurationinseconds	**0,05**	0,69
mediumstressdurationinseconds	**0,04**	0,78
highstressdurationinseconds	**<0.001**	0,72

Table 7. ANOVA test results for dailies summaries - Subj 1

DAILIES	**P-VALUE**
steps	0,82
distanceinmeters	0,61
activetimeinseconds	0,52
floorsclimbed	0,35
activekilocalories	**0,007**
moderateintensitydurationinseconds	0,42
vigorousintensitydurationinseconds	0,42
minheartrateinbeatsperminute	0,26
averageheartrateinbeatsperminute	0,09
maxheartrateinbeatsperminute	0,68
stdheartrate15seconds	**0,02**
restingheartrateinbeatsperminute	0,57
averagestresslevel	0,07
maxstresslevel	**0.05**
stressdurationinseconds	**0,05**
reststressdurationinseconds	**0,03**
activitystressdurationinseconds	0,47
lowstressdurationinseconds	**0,11**
mediumstressdurationinseconds	0,30
highstressdurationinseconds	0,33

Table 8. Tukey's test results for dailies summaries - Subj 1

activeKilocalories
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,83	False
1	3	0,63	False
1	4	0,01	True
1	5	0,03	True
2	3	0,1	False
2	4	0,13	False
2	5	0,27	False
3	4	0,25	False
3	5	0,44	False
4	5	0,99	False

stdHeartRate15Seconds
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,99	False
1	3	0,94	False
1	4	0,17	False
1	5	0,32	False
2	3	0,88	False
2	4	0,23	False
2	5	0,40	False
3	4	0,04	True
3	5	0,08	False
4	5	0.99	False

averageStressLevel
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,26	False
1	3	0,66	False
1	4	0,39	False
1	5	0,04	True
2	3	0,95	False
2	4	0,99	False
2	5	0,90	False
3	4	0,99	False
3	5	0,51	False
4	5	0,78	False

stressDurationInSeconds
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,15	False
1	3	0,44	False
1	4	0,28	False
1	5	0,02	True
2	3	0,96	False
2	4	0,99	False
2	5	0,92	False
3	4	0,99	False
3	5	0,05	False
4	5	0,77	False

restStressDurationInSeconds
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,2	False
1	3	0,97	False
1	4	0,54	False
1	5	0,02	True
2	3	0,51	False
2	4	0,96	False
2	5	0,86	False
3	4	0,88	False
3	5	0,10	False
4	5	0,48	False

Table 9. ANOVA assumption results for sleep summaries - Subj 1

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
durationInSeconds	0,73	0,61
deepSleepDurationInSeconds	**<0,001**	0,46
lightSleepDurationInSeconds	0,09	0,60
remSleepDurationInSeconds	0,99	0,76
awakeDurationInSeconds	**<0,001**	0,46
Deep_sleep_episodes	<0,001	0,70
Light_sleep_episodes	0,06	0,70
Rem_sleep_episodes	0,09	0,20
Awake_sleep_episodes	**0,01**	0,81

Table 10. ANOVA results for sleep summaries - Subj 1

SLEEP	**P-VALUE**
durationInSeconds	0,36
deepSleepDurationInSeconds	0,63
lightSleepDurationInSeconds	0,07
remSleepDurationInSeconds	0,46
awakeDurationInSeconds	0,31
Deep_sleep_episodes	0,43
Light_sleep_episodes	0,37
Rem_sleep_episodes	0,17
Awake_sleep_episodes	0,45

Table 11. ANOVA assumption results for stress summaries – Subj 1

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
max_timeOffsetStressLevelValues	0,16	0,85
min_timeOffsetStressLevelValues	**<0,001**	0,56
median_timeOffsetStressLevelValues	**<0,001**	0,41
mean_timeOffsetStressLevelValues	0,07	0,97
std_timeOffsetstresslevelvalues	0,06	0,97
perc25_ timeOffsetstresslevelvalues	0,63	0,97
perc50_ timeOffsetstresslevelvalues	**<0,001**	0,41
perc75_ timeOffsetstresslevelvalues	**0,01**	0,97
max_timeOffsetBodyBatteryValues	**<0,001**	0,56
min_ timeOffsetBodyBatteryValues	**0,05**	0,42
median_ timeOffsetBodyBatteryValues	0,98	0,74
mean_ timeOffsetBodyBatteryValues	0,88	0,92
std_ timeOffsetBodyBatteryValues	0,95	0,47
perc25_ timeOffsetBodyBatteryValues	0,83	0,81
perc50_ timeOffsetBodyBatteryValues	0,98	0,75
perc75_ timeOffsetBodyBatteryValues	**0,01**	0,91

Table 12. ANOVA results for stress summaries – Subj 1

STRESS	**P-VALUE**
max_timeOffsetStressLevelValues	0,80
min_timeOffsetStressLevelValues	0,21
median_timeOffsetStressLevelValues	**0,02**
mean_timeOffsetStressLevelValues	**0,05**
std_timeOffsetstresslevelvalues	**0,64**
perc25_ timeOffsetstresslevelvalues	**0,02**
perc50_ timeOffsetstresslevelvalues	**0,02**
perc75_ timeOffsetstresslevelvalues	0,07
max_timeOffsetBodyBatteryValues	**0,07**
min_ timeOffsetBodyBatteryValues	**0,003**
median_ timeOffsetBodyBatteryValues	**0,01**
mean_ timeOffsetBodyBatteryValues	**0,01**
std_ timeOffsetBodyBatteryValues	0,33
perc25_ timeOffsetBodyBatteryValues	**0,01**
perc50_ timeOffsetBodyBatteryValues	**0,01**
perc75_ timeOffsetBodyBatteryValues	**0,05**

Table 13. Tukey's test results for stress summaries – Subj 1

median_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,02	True
1	3	0,47	False
1	4	0,53	False
1	5	0,03	True
2	3	0,47	False
2	4	0,42	False
2	5	1	False
3	4	1	False
3	5	0,57	False
4	5	0,51	False

perc50_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,02	True
1	3	0,47	False
1	4	0,53	False
1	5	0,04	True
2	3	0,47	False
2	4	0,42	False
2	5	1,0	False
3	4	1,0	False
3	5	0,57	False
4	5	0,52	False

min_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,72	False
1	3	0,98	False
1	4	0,48	False
1	5	0,002	True
2	3	0,95	False
2	4	0,99	False
2	5	0,03	True
3	4	0,81	False
3	5	0,008	True
4	5	0,08	False

median_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,62	False
1	3	0,99	False
1	4	0,87	False
1	5	0,01	True
2	3	0,81	False
2	4	0,99	False
2	5	0,18	False
3	4	0,96	False
3	5	0,02	True
4	5	0,08	False

mean_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,71	False
1	3	0,99	False
1	4	0,97	False
1	5	0,01	True
2	3	0,63	False
2	4	0,95	False
2	5	0,17	False
3	4	0,95	False
3	5	0,01	True
4	5	0,04	True

perc25_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,91	False
1	3	1,0	False
1	4	0,69	False
1	5	0,01	True
2	3	0,90	False
2	4	0,99	False
2	5	0,06	False
3	4	0,67	False
3	5	0,01	True
4	5	0,16	False

perc50_timeOffsetBodyBatteryValues Tukey HSD, FWER = 0.05			
Group1	Group2	p-adj	Sig.
1	2	0,6	False
1	3	0,99	False
1	4	0,87	False
1	5	0,01	True
2	3	0,81	False
2	4	0,99	False
2	5	0,18	False
3	4	0,97	False
3	5	0,02	True
4	5	0,08	False

Table 14. ANOVA test assumption results for dailies summaries – Subj 2

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
steps	0,55	0,80
distanceinmeters	0,33	0,84
activetimeinseconds	0,80	0,88
floorsclimbed	**<0,001**	0,55
activekilocalories	**0,005**	0,80
moderateintensitydurationinseconds	**<0,001**	0,46
vigorousintensitydurationinseconds	**<0,001**	0,67
minheartrateinbeatsperminute	0,23	0,93
averageheartrateinbeatsperminute	**0,009**	0,21
maxheartrateinbeatsperminute	**0,04**	0,54
stdheartrate15seconds	0,71	0,71
restingheartrateinbeatsperminute	0,13	0,63
averagestresslevel	**0,003**	0,47
maxstresslevel	0,06	0,90
stressdurationinseconds	**0,002**	0,30
reststressdurationinseconds	**0,02**	0,67
activitystressdurationinseconds	**0,001**	0,30
lowstressdurationinseconds	0,07	0,65
mediumstressdurationinseconds	**<0,001**	0,20
highstressdurationinseconds	**<0,001**	0,31

Table 15. ANOVA test results for dailies summaries – Subj 2

DAILIES	**P-VALUE**
steps	**<0,001**
distanceinmeters	**<0,001**
activetimeinseconds	**0,01**
floorsclimbed	0,62
activekilocalories	0,86
moderateintensitydurationinseconds	0.15
vigorousintensitydurationinseconds	0.67
minheartrateinbeatsperminute	0,14
averageheartrateinbeatsperminute	0,07
maxheartrateinbeatsperminute	0.19
stdheartrate15seconds	0,84
restingheartrateinbeatsperminute	**<0,001**
averagestresslevel	**0,04**
maxstresslevel	0,39
stressdurationinseconds	**<0.001**
reststressdurationinseconds	**0,03**
activitystressdurationinseconds	0,12
lowstressdurationinseconds	**<0,001**
mediumstressdurationinseconds	0,06
highstressdurationinseconds	0,23

Table 16. Tukey's test results for dailies summaries – Subj 2

steps
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,03	True
1	3	0,83	False
1	4	0,61	False
1	5	0,99	False
2	3	0,24	False
2	4	0,001	True
2	5	0,07	False
3	4	0,13	False
3	5	0,96	False
4	5	0,39	False

distanceInMeters
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,03	True
1	3	0,83	False
1	4	0,61	False
1	5	0,99	False
2	3	0,24	False
2	4	0,001	True
2	5	0,07	False
3	4	0,13	False
3	5	0,96	False
4	5	0,39	False

activeTimeInSeconds
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,09	False
1	3	0,49	False
1	4	0,76	False
1	5	0,87	False
2	3	0,82	False
2	4	0,008	True
2	5	0,44	False
3	4	0,07	False
3	5	0,96	False
4	5	0,25	False

restingHeartRateInBeatsPerMinute
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,90	False
1	3	0,59	False
1	4	0,01	True
1	5	0,02	True
2	3	0,98	False
2	4	0,10	False
2	5	0,20	False
3	4	0,24	False
3	5	0,42	False
4	5	0,99	False

averageStressLevel
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,99	False
1	3	0,99	False
1	4	0,85	False
1	5	0,10	False
2	3	0,97	False
2	4	0,93	False
2	5	0,18	False
3	4	0,63	False
3	5	0,04	True
4	5	0,59	False

stressDurationInSeconds
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,99	False
1	3	1.0	False
1	4	0.10	False
1	5	0,03	True
2	3	0,99	False
2	4	0,18	False
2	5	0,08	False
3	4	0,10	False
3	5	0,04	True
4	5	0,99	False

restStressDurationInSeconds Tukey HSD, FWER = 0.05			
Group1	Group2	p-adj	Sig.
1	2	1.0	False
1	3	0.99	False
1	4	0.71	False
1	5	0.10	False
2	3	0,99	False
2	4	0,66	False
2	5	0,10	False
3	4	0,48	False
3	5	0,05	True
4	5	0,76	False

lowStressDurationInSeconds Tukey HSD, FWER = 0.05			
Group1	Group2	p-adj	Sig.
1	2	0,30	False
1	3	0,69	False
1	4	0,13	False
1	5	0,11	False
2	3	0,94	False
2	4	0,002	True
2	5	0,001	True
3	4	0,008	True
3	5	0,005	True
4	5	1	False

Table 17. ANOVA assumption results for sleep summaries – Subj 2

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
durationInSeconds	**<0,001**	0,46
deepSleepDurationInSeconds	0,26	0,71
lightSleepDurationInSeconds	**0,004**	0,50
remSleepDurationInSeconds	0,07	0,73
awakeDurationInSeconds	**<0,001**	0,36
Deep_sleep_episodes	**0,006**	0,70
Light_sleep_episodes	0,13	**0,05**
Rem_sleep_episodes	0,06	0,63
Awake_sleep_episodes	**0,002**	0,89

Table 18. ANOVA results for sleep summaries – Subj 2

SLEEP	**P-VALUE**
durationInSeconds	0,63
deepSleepDurationInSeconds	0,56
lightSleepDurationInSeconds	0,83
remSleepDurationInSeconds	0,96
awakeDurationInSeconds	0,48
Deep_sleep_episodes	0,71
Light_sleep_episodes	0,21
Rem_sleep_episodes	0,10
Awake_sleep_episodes	0,75

Table 19. ANOVA assumption results for stress summaries – Subj 2

	NORMAL DISTRIBUTION	***HOMOGENEITY OF VARIANCE***
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
max_timeOffsetStressLevelValues	**0,009**	0,40
min_timeOffsetStressLevelValues	**<0,001**	0,38
median_timeOffsetStressLevelValues	**<0,001**	0,31
mean_timeOffsetStressLevelValues	**<0,001**	0,18
std_timeOffsetstresslevelvalues	0,30	0,34
perc25_ timeOffsetstresslevelvalues	**<0,001**	0,27
perc50_ timeOffsetstresslevelvalues	**<0,001**	0,31
perc75_ timeOffsetstresslevelvalues	**0,004**	0,34
max_timeOffsetBodyBatteryValues	**<0,001**	0,16
min_ timeOffsetBodyBatteryValues	**0,007**	0,87
median_ timeOffsetBodyBatteryValues	**0,01**	0,42
mean_ timeOffsetBodyBatteryValues	**0,003**	0,35
std_ timeOffsetBodyBatteryValues	**0,04**	0,30
perc25_ timeOffsetBodyBatteryValues	**0,004**	0,76
perc50_ timeOffsetBodyBatteryValues	**0,01**	0,42
perc75_ timeOffsetBodyBatteryValues	**0,005**	0,32

Table 20. ANOVA results for stress summaries – Subj 2

STRESS	**P-VALUE**
max_timeOffsetStressLevelValues	0,50
min_timeOffsetStressLevelValues	0,17
median_timeOffsetStressLevelValues	**0,003**
mean_timeOffsetStressLevelValues	**0,004**
std_timeOffsetstresslevelvalues	0,10
perc25_ timeOffsetstresslevelvalues	**0,008**
perc50_ timeOffsetstresslevelvalues	**0,003**
perc75_ timeOffsetstresslevelvalues	**0,002**
max_timeOffsetBodyBatteryValues	**0,005**
min_ timeOffsetBodyBatteryValues	**<0,001**
median_ timeOffsetBodyBatteryValues	**<0,001**
mean_ timeOffsetBodyBatteryValues	**0,01**
std_ timeOffsetBodyBatteryValues	**0,001**
perc25_ timeOffsetBodyBatteryValues	**<0,001**
perc50_ timeOffsetBodyBatteryValues	**0,003**

Table 21. Tukey's test results for stress summaries – Subj 2

median_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,61	False
1	3	0,60	False
1	4	0,16	False
1	5	0,17	False
2	3	0,05	False
2	4	0,86	False
2	5	0,85	False
3	4	0,007	True
3	5	0,009	True
4	5	1.0	False

mean_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,77	False
1	3	0,75	False
1	4	0,26	False
1	5	0,08	False
2	3	0,15	False
2	4	0,87	False
2	5	0,50	False
3	4	0,02	True
3	5	0,006	True
4	5	0,96	False

perc25_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,61	False
1	3	0,95	False
1	4	0,09	False
1	5	0,15	False
2	3	0,24	False
2	4	0,70	False
2	5	0,82	False
3	4	0,022	True
3	5	0,04	True
4	5	0,99	False

perc50_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,62	False
1	3	0,60	False
1	4	0,16	False
1	5	0,17	False
2	3	0,06	False
2	4	0,86	False
2	5	0,85	False
3	4	0,007	True
3	5	0,009	True
4	5	1.0	False

perc75_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,96	False
1	3	0,49	False
1	4	0,37	False
1	5	0,07	False
2	3	0,18	False
2	4	0,74	False
2	5	0,23	False
3	4	0,01	True
3	5	0,002	True
4	5	0,87	False

max_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,98	False
1	3	0,62	False
1	4	0,19	False
1	5	0,20	False
2	3	0,32	False
2	4	0,43	False
2	5	0,42	False
3	4	0,01	True
3	5	0,01	True
4	5	1.0	False

min_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,69	False
1	3	0,99	False
1	4	0,05	True
1	5	0,002	True
2	3	0,76	False
2	4	0,46	False
2	5	0,03	True
3	4	0,06	False
3	5	0,002	True
4	5	0,59	False

median_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,88	False
1	3	0,81	False
1	4	0,05	False
1	5	0,03	True
2	3	0,28	False
2	4	0,29	False
2	5	0,18	False
3	4	0,004	True
3	5	0,003	True
4	5	0,99	False

mean_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,90	False
1	3	0,87	False
1	4	0,06	False
1	5	0,03	True
2	3	0,37	False
2	4	0,31	False
2	5	0,18	False
3	4	0,007	True
3	5	0,004	True
4	5	0,99	False

std_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	1.0	False
1	3	0,26	False
1	4	0,51	False
1	5	0,95	False
2	3	0,27	False
2	4	0,49	False
2	5	0,93	False
3	4	0,01	True
3	5	0,09	False
4	5	0,94	False

perc25_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,71	False
1	3	1.0	False
1	4	0,03	True
1	5	0,006	True
2	3	0,62	False
2	4	0,36	False
2	5	0,08	False
3	4	0,02	True
3	5	0,004	True
4	5	0,91	False

perc50_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,88	False
1	3	0,81	False
1	4	0,05	False
1	5	0,03	True
2	3	0,28	False
2	4	0,29	False
2	5	0,18	False
3	4	0,004	True
3	5	0,003	True
4	5	0,99	False

perc75_timeOffsetBodyBatteryValues Tukey HSD, FWER = 0.05			
Group1	Group2	p-adj	Sig.
1	2	0,97	False
1	3	0,65	False
1	4	0,12	False
1	5	0,15	False
2	3	0,29	False
2	4	0,34	False
2	5	0,39	False
3	4	0,006	True
3	5	0,01	True
4	5	1.0	False

Table 22. ANOVA test assumption results for dailies summaries -Subj 3

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
steps	0,88	0,65
distanceinmeters	0,84	0,75
activetimeinseconds	0,44	0,56
floorsclimbed	**0,05**	**0,03**
activekilocalories	0,97	0,72
moderateintensitydurationinseconds	**0,006**	0,80
vigorousintensitydurationinseconds	**<,001**	0,41
minheartrateinbeatsperminute	0,55	0,36
averageheartrateinbeatsperminute	0,27	0,31
maxheartrateinbeatsperminute	**<,001**	0,82
stdheartrate15seconds	0,80	0,70
restingheartrateinbeatsperminute	0,05	0,39
averagestresslevel	0,36	0,58
maxstresslevel	0,07	0,68
stressdurationinseconds	0,46	0,86
reststressdurationinseconds	0,82	0,59
activitystressdurationinseconds	0,41	0,94
lowstressdurationinseconds	0,56	0,90
mediumstressdurationinseconds	**0,02**	0,19
highstressdurationinseconds	**<,001**	0,13

Table 23. ANOVA test results for dailies summaries -Subj 3

DAILIES	**P-VALUE**
steps	0.84
distanceInMeters	0.85
activeTimeInSeconds	0.93
activeKilocalories	0.99
moderateIntensityDurationInSeconds	0.90
vigorousIntensityDurationInSeconds	0.41
minHeartRateInBeatsPerMinute	**0.01**
averageHeartRateInBeatsPerMinute	**0.003**
maxHeartRateInBeatsPerMinute	0.95
stdheartrate15seconds	0.65
restingHeartRateInBeatsPerMinute	**0.01**
averageStressLevel	**0.0009**
maxStressLevel	0.60
stressDurationInSeconds	**0.02**
restStressDurationInSeconds	**0.006**
activityStressDurationInSeconds	0.50
lowStressDurationInSeconds	0.07
mediumStressDurationInSeconds	**0.03**
highStressDurationInSeconds	0.13

Table 24. Tukey's test results for dailies summaries -Subj 3

minHeartRateInBeatsPerMinute
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,26	False
1	3	0,63	False
1	4	0,24	False
2	3	0,02	True
2	4	0,10	False
3	4	0,02	True

averageHeartRateInBeatsPerMinute
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,02	True
1	3	0,97	False
1	4	0,01	True
2	3	0,07	False
2	4	0,97	False
3	4	0,02	True

restingHeartRateInBeatsPerMinute
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,03	True
1	3	0,10	False
1	4	0,19	False
2	3	0,03	True
2	4	0,79	False
3	4	0,17	False

averageStressLevel
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,10	False
1	3	0,04	True
1	4	0,98	False
2	3	0,53	False
2	4	0,05	False
3	4	0,002	True

stressDurationInSeconds
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,03	True
1	3	0,13	False
1	4	0,98	False
2	3	0,89	False
2	4	0,06	False
3	4	0,22	False

restStressDurationInSeconds
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,26	False
1	3	0,01	True
1	4	0,99	False
2	3	0,42	False
2	4	0,31	False
3	4	0,01	True

mediumStressDurationInSeconds
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2		False
1	3		False
1	4		False
2	3		False
2	4		False
3	4		False

Table 25. ANOVA assumption results for sleep summaries -Subj 3

	NORMAL DISTRIBUTION	HOMOGENEITY OF VARIANCE
	Shapiro-Wilk test: p-value	**Leneve's test: p-value**
durationInSeconds	0.78	0,72
deepSleepDurationInSeconds	0.03	0,80
lightSleepDurationInSeconds	0,02	0,68
remSleepDurationInSeconds	0,39	0,90
awakeDurationInSeconds	<0,01	0,36
Deep_sleep_episodes	0,20	0,44
Light_sleep_episodes	0,33	0,73
Rem_sleep_episodes	0,89	0,26
Awake_sleep_episodes	<0,01	0,37

Table 26. ANOVA results for sleep summaries -Subj 3

SLEEP	P-VALUE
durationInSeconds	0.47
deepSleepDurationInSeconds	0.42
lightSleepDurationInSeconds	0.91
remSleepDurationInSeconds	0.09
awakeDurationInSeconds	0.22
Deep_sleep_episodes	0.15
Light_sleep_episodes	0.05
Rem_sleep_episodes	0.39
Awake_sleep_episodes	0.96

Table 27. Tukey's test results for sleep summaries – Subj 3

Light_sleep episodes
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,82	False
1	3	0,04	True
1	4	0,37	False
2	3	0,21	False
2	4	0,84	False
3	4	0,69	False

Table 28. ANOVA assumption results for stress summaries – Subj 3

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	**Leneve's test: p-value**
max_timeOffsetStressLevelValues	0,57	0,33
min_timeOffsetStressLevelValues	<0.01	0,03
median_timeOffsetStressLevelValues	0,07	0,05
mean_timeOffsetStressLevelValues	0,29	0,46
std_timeOffsetstresslevelvalues	0,75	0,11
perc25_ timeOffsetstresslevelvalues	0,21	0,34
perc50_ timeOffsetstresslevelvalues	0,07	0,05
perc75_ timeOffsetstresslevelvalues	0,24	0,64
max_timeOffsetBodyBatteryValues	0,08	0,45
min_ timeOffsetBodyBatteryValues	0,74	0,98
median_ timeOffsetBodyBatteryValues	0,74	0,71
mean_ timeOffsetBodyBatteryValues	0,39	0,45
std_ timeOffsetBodyBatteryValues	0,34	0,98
perc25_ timeOffsetBodyBatteryValues	0,61	0,89
perc50_ timeOffsetBodyBatteryValues	0,74	0,71
perc75_ timeOffsetBodyBatteryValues	0,60	0,32

Table 29. ANOVA results for stress summaries – Subj 3

STRESS	**P-VALUE**
max_timeOffsetStressLevelValues	0,48
median_timeOffsetStressLevelValues	**< 0,01**
mean_timeOffsetStressLevelValues	**< 0,01**
std_timeOffsetstresslevelvalues	**< 0,01**
perc25_ timeOffsetstresslevelvalues	**< 0,01**
perc50_ timeOffsetstresslevelvalues	**< 0,01**
perc75_ timeOffsetstresslevelvalues	**< 0,01**
max_timeOffsetBodyBatteryValues	**0,03**
min_ timeOffsetBodyBatteryValues	**< 0,01**
median_ timeOffsetBodyBatteryValues	**0,01**
mean_ timeOffsetBodyBatteryValues	**< 0,01**
std_ timeOffsetBodyBatteryValues	0,32
perc25_ timeOffsetBodyBatteryValues	**< 0,01**
perc50_ timeOffsetBodyBatteryValues	**0,01**
perc75_ timeOffsetBodyBatteryValues	**0,03**

Table 30. Tukey's test results for stress summaries – Subj 3

median_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,20	False
1	3	0,04	Ture
1	4	0,77	False
2	3	0,88	False
2	4	0,02	True
3	4	0,005	True

mean_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,07	False
1	3	0,006	True
1	4	0,99	False
2	3	0,68	False
2	4	0,04	True
3	4	0,003	True

std_timeOffsetstresslevelvalues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,02	True
1	3	0,01	True
1	4	0,21	False
2	3	0,99	False
2	4	0,60	False
3	4	0,56	False

perc25_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,69	False
1	3	0,06	False
1	4	0,64	False
2	3	0,45	False
2	4	0,13	False
3	4	0,004	True

perc50_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,20	False
1	3	0,04	True
1	4	0,77	False
2	3	0,88	False
2	4	0,03	True
3	4	0,005	True

perc75_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,12	False
1	3	0,02	True
1	4	1.0	False
2	3	0.86	False
2	4	0.12	False
3	4	0.02	True

min_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,02	True
1	3	0,002	True
1	4	0,46	False
2	3	0,77	False
2	4	0,36	False
3	4	0,66	False

median_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,22	False
1	3	0,01	True
1	4	0,95	False
2	3	0,51	False
2	4	0,48	False
3	4	0,04	True

mean_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,18	False
1	3	0,01	True
1	4	0,98	False
2	3	0,54	False
2	4	0,34	False
3	4	0,03	True

perc25_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,07	False
1	3	0,004	True
1	4	0,97	False
2	3	0,62	False
2	4	0,29	False
3	4	0,02	True

perc50_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,22	False
1	3	0,01	True
1	4	0,94	False
2	3	0,51	False
2	4	0,49	False
3	4	0.04	True

perc75_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,55	False
1	3	0,05	False
1	4	0,99	False
2	3	0,53	False
2	4	0,48	False
3	4	0,04	True

Table 31. ANOVA test assumption results for dailies summaries – Subj 4

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
steps	0,96	0,86
distanceinmeters	0,86	0,81
activetimeinseconds	0,51	0,41
floorsclimbed	0,40	0,90
activekilocalories	0,75	0,74
moderateintensitydurationinseconds	**<,001**	0,38
vigorousintensitydurationinseconds	**<0,001**	0,17
minheartrateinbeatsperminute	0,06	0,47
averageheartrateinbeatsperminute	0,70	0,22
maxheartrateinbeatsperminute	0,94	0,96
stdheartrate15seconds	0,27	0,58
restingheartrateinbeatsperminute	0,11	0,43
averagestresslevel	0,95	0,81
maxstresslevel	0,34	0,98
stressdurationinseconds	0,73	0,86
reststressdurationinseconds	0,44	0,64
activitystressdurationinseconds	**0,01**	0,06
lowstressdurationinseconds	0,35	0,97
mediumstressdurationinseconds	0,61	0,71
highstressdurationinseconds	**0,004**	0,85

Table 32. ANOVA results for dailies summaries – Subj 4

DAILIES	**P-VALUE**
steps	0,16
distanceinmeters	0,23
activetimeinseconds	0,51
floorsclimbed	0,58
activekilocalories	0,40
moderateintensitydurationinseconds	0,39
vigorousintensitydurationinseconds	0,17
minheartrateinbeatsperminute	0,63
averageheartrateinbeatsperminute	0.21
maxheartrateinbeatsperminute	0.12
stdheartrate15seconds	0,55
restingheartrateinbeatsperminute	0,85
averagestresslevel	0,06
maxstresslevel	0,47
stressdurationinseconds	**0,05**
reststressdurationinseconds	0,10
activitystressdurationinseconds	0,78
lowstressdurationinseconds	0,23
mediumstressdurationinseconds	**0,007**
highstressdurationinseconds	0,70

Table 33. Tukey's test results for dailies summaries – Subj 4

mediumStressDurationInSeconds Tukey HSD, FWER = 0.05			
Group1	Group2	p-adj	Sig.
1	2	0,99	False
1	3	0,75	False
1	4	0,02	True
2	3	0,73	False
2	4	0,001	True
3	4	0,08	False

Table 34. ANOVA test assumptions results – Subj 4

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
DurationInSeconds	0.82	0,27
DeepSleepDurationInSeconds	**<,001**	0,81
LightSleepDurationInSeconds	0,13	0,99
RemSleepInSeconds	0,17	0,46
AwakeDurationInSeconds	**0,06**	0,92
Deep_sleep_episodes	**<,001**	0,98
Light_sleep_episodes	0,35	0,27
Rem_sleep_episodes	0,62	0,65
Awake_sleep_episodes	**0,02**	0,72

Table 35. ANOVA sleep results – Subj 4

SLEEP	**P-VALUE**
DurationInSeconds	0,51
DeepSleepDurationInSeconds	0,76
LightSleepDurationInSeconds	0,23
RemSleepInSeconds	0,93
AwakeDurationInSeconds	0,47
Deep_sleep_episodes	0,62
Light_sleep_episodes	0,59
Rem_sleep_episodes	0,82
Awake_sleep_episodes	0,29

Table 36. Anova stress assumptions result – Subj 4

	NORMAL DISTRIBUTION	**HOMOGENEITY OF VARIANCE**
	Shapiro-Wilk test: p-value	***Leneve's test: p-value***
max_timeOffsetStressLevelValues	**<,001**	0,33
min_timeOffsetStressLevelValues	**<,001**	0,17
median_timeOffsetStressLevelValues	0,20	0,89
mean_timeOffsetStressLevelValues	0,79	0,97
std_timeOffsetStressLevelValues	**0,002**	0,36
perc25_timeoffsetstresslevelvalues	**0,004**	0,35
perc50_timeoffsetstresslevelvalues	0,20	0,89
perc75_timeoffsetstresslevelvalues	0,70	0,78
max_timeOffsetBodyBatteryValues	**<,001**	0,14
min_timeOffsetBodyBatteryValues	**<,001**	0,12
median_timeOffsetBodyBatteryValues	0,45	0,76
mean_timeOffsetBodyBatteryValues	0,95	0,78
std_timeOffsetBodyBatteryValues	0,26	0,81
perc25_timeoffsetbodybatteryvalues	**<,001**	0,28
perc50_timeoffsetbodybatteryvalues	0,45	0,76
perc75_timeoffsetbodybatteryvalues	0,62	0,83

Table 37. ANOVA stress result – Subj 4

STRESS	**P-VALUE**
max_timeOffsetStressLevelValues	**0,001**
min_timeOffsetStressLevelValues	0,12
median_timeOffsetStressLevelValues	0,18
mean_timeOffsetStressLevelValues	0,41
std_timeOffsetStressLevelValues	**0,03**
perc25_timeoffsetstresslevelvalues	0,11
perc50_timeoffsetstresslevelvalues	0,17
perc75_timeoffsetstresslevelvalues	0,63
max_timeOffsetBodyBatteryValues	**<,001**
min_timeOffsetBodyBatteryValues	0,12
median_timeOffsetBodyBatteryValues	0,25
mean_timeOffsetBodyBatteryValues	0,27
std_timeOffsetBodyBatteryValues	**0,04**
perc25_timeoffsetbodybatteryvalues	0,31
perc50_timeoffsetbodybatteryvalues	0,25
perc75_timeoffsetbodybatteryvalues	0,41

Table 38. Tukey's test results for stress summaries – Subj 4

max_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,001	True
1	3	0,01	True
1	4	0,007	True
2	3	0,77	False
2	4	0,90	False
3	4	0,99	False

std_timeOffsetStressLevelValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,02	True
1	3	0,09	False
1	4	0,12	False
2	3	0,90	False
2	4	0,85	False
3	4	0,99	False

max_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,001	True
1	3	0,004	True
1	4	0,002	True
2	3	0,96	False
2	4	0,99	False
3	4	0,99	False

std_timeOffsetBodyBatteryValues
Tukey HSD, FWER = 0.05

Group1	Group2	p-adj	Sig.
1	2	0,04	True
1	3	0,17	False
1	4	0,65	False
2	3	0,86	False
2	4	0,33	False
3	4	0,77	False