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Late Life Depression: The Role of Motion Detection Technology in Diagnosis and Management

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Case presentation

“Mr. G” is an 81-year-old Caucasian male with a history of mild neurocognitive disorder and unspecified bipolar, or related disorder with atypical features (mood reactivity), who was referred by his neurologist for geriatric psychiatry assessment . The patient presented with a complicated medical history including carotid stenosis with transient ischemic attacks (post stenting) and throat cancer which required radiation treatment, which, in turn, resulted in subsequent mandibular osteonecrosis. The patient also had squamous cell carcinomas post resection, low testosterone requiring supplementation, hypertension and hypercholesterolemia. At the time of his initial presentation, the patient's primary complaint was "my head feels as if it is in a fog." It was noteworthy that this patient was both affluent and very high functioning at baseline and ran a large business. He had concerns about his ability to function at his work. A review of his medications indicated that he was taking aripiprazole 2 mg once a week and fluoxetine 20 mg daily for depression. He was also taking four additional medications at bedtime for insomnia - melatonin 2.5 mg, temazepam 15 mg, mirtazapine 15 mg and zaleplon 10 mg - all taken. His non-psychotropic medications included amlodipine 5 mg daily, aspirin 81 mg daily, levothyroxine 150 mcg daily, lisinopril 10 mg daily, lovastatin 40 mg daily, tamsulosin 0.4 mg at bedtime and testosterone supplementation. The patient scored 20 out of a maximum possible score of 30, on the Montreal Cognitive Assessment (MOCA)(do we

need to include a reference for the MOCA?) indicating mild neurocognitive disorder. A review of his performance on a previous administration of the MOCA indicated that his score had dropped by 6 points over the preceding 14 months.

The patient had ben diagnosed with severe carotid stenosis one year prior to presentation. He reported that he had experienced an episode of dizziness and hypoxia, which led to this diagnoses. His carotid arteries had required emergent stenting. Subsequently, he developed a major depressive episode and was treated with fluoxetine 40 mg q. daily and aripiprazole 5 mg q. daily, however, this precipitated what was described as a hypomanic episode, whose defining features included impulsive business decisions, pressured speech and insomnia. As a result, he was taken off fluoxetine and aripiprazole and his hypomania resolved. Approximately 2 months prior to presentation, he demonstrated some amotivation and low energy, and was restarted on 20 mg of fluoxetine by his primary care physician, but with minimal effect.

The patient’s physical examination revealed orthostatic hypotension, but his vitals were otherwise within normal range. A comprehensive laboratory investigation, which included a complete blood count with differential analysis, a comprehensive metabolic panel, liver function tests, cardiac workup, and assessment for hypothyroidism, hypogonadism and low vitamin levels, was found to be noncontributory. A volumetric MRI of his brain demonstrated stable age related volume loss and superimposed white

matter changes suggesting chronic microvascular ischemia, but was otherwise found to be normal. His hippocampal volume was found to be higher than the 5th percentile and his lateral ventricular volume was at the 79th percentile, both within normal limits.

Mr. G was relatively nonspecific when describing his clinical complains, using terms like "my brain is in a fog" and reported both hypersomnia as well as insomnia at different points in the initial assessment. His wife, who was present during the initial as well as subsequent sessions, provided reliable collateral information, but stated that she was not always around him and not always observing him. He denied depressed mood, episodes of tearfulness, anhedonia, feelings of worthlessness, changes in appetite, and thoughts of death or fatigue. There was no initial reported history of psychomotor retardation.

Polypharmacy was identified as a primary clinical issue initially and zaleplon and melatonin were discontinued. His mirtazapine dose was reduced to 7.5 mg at bedtime, but he reported recurrence of insomnia, and his was returned to 15 mg. Mr. G noted that he had been on temazepam for over 30 years and had relied on this for sleep. He became anxious at the notion of tapering off this medication and so a decision was made to defer this to a later time. Despite being on this medication for several years, the reported confusion and “brain fog” were a relatively recent complaints. In consultation with the patient's primary care provider, to address the patient's hypotension his amlodipine was incrementally discontinued, but this resulted

in an exacerbation of hypertension, with his blood pressure hitting a high of 214/112 mm Hg. Subsequently, amlodipine was restarted at a lower dose of 2.5 mg per day, which resulted in successful management of his hypertension without hypotension.

Assessment of Mr. G’s level of functioning suggested ongoing confusion and poor decision making over the course of the first after resuming treatment with fluoxetine.. This was the primary complaint ofthe patient and his wife, both of whom repeatedly said they were concerned about his ability to manage his business due to his current mental state.

Because of unclear objective information about the patient's sleep pattern, a recommendation was made for the patient to use a wrist worn actigraph, several of which are commercially available and utilize accelerometry to record motion, as well as sleep. The patient was receptive to this idea and purchased a device called “Up,” manufactured by the company, Jawbone. The patient received educaion on how to use this device to keep track of his daily step count, to record his sleep, and to synchronize it with his smart phone (the device manufacturers have developed an app that allows seamless transmission of data to a smart phone or tablet for visualization of data).

After monitoring for one week, at the next clinic visit, it was noted that the patient had slept for an average of 8-9 hours of good quality sleep, ruling out insomnia,however, a review of his daytime motion data indicated that over the preceding 5 days, the patient had only taken an average of 836 steps

per day. Moreover, this number was driven by a single day that he had taken a long walk, at the insistence of his wife. After excluding this day, the average number of steps for the remaining days was 440 (screenshot of patient's cellphone is included as Figure 1).

---------- Insert Figure 1 here----------

Further inquiry revealed that the patient lived in a very large house, and this step count was achieved simply by going from his bedroom to the bathroom, or the dining room for meals, and that the patient was spending the majority of his day lying in bed.

This newly-identified severe psychomotor retardation, in combination with previously reported evidence of poor energy , low motivation, indecisiveness andconfusion, and objective evidence of adequate sleep, led us to reconsider the treatment plan. His dose of fluoxetine was increased to 40 mg per day, and aripiprazole augmentation at 2 mg per day was initiated. Over the course of the next 3 weeks, Mr. G demonstrated improvement in mood as well as energy. His accelerometer data continued to be monitored, and revealed that his average step count increased to approximately 4000 steps per day.

Discussion

It has been well established that the depressive symptoms in late life can be challenging to diagnose because of heterogeneity of clinical presentation

(1,2). Moreover, older adults frequently fail to meet *Diagnostic and Statistical Manual (DSM)* criteria for depressive episodes. Older adults also frequently present with subsyndromal depressive symptoms and the prevalence of subsyndromal depression may be up to 3 times higher than major depression in this population (3,4). In older adults like Mr. G, with comorbid mood symptoms and cognitive impairment, reliable clinical information, as well as collateral information, may be unreliable or biased. This case highlights how motion-sensing technology can impact several dimensions of diagnosis and management of depressive symptoms in late life by providing a more accurate clinical understanding of specific factors that can be key determinants of care. Currently available devices are able, at a minimum, to provide quantified information on sleep and physical activity, both of which are diagnostically pertinent factors for clinicians.

Sleep Disturbances and Depression

Sleep disruption in older adults may include insomnia (over 30 minutes to fall asleep, or waking up earlier than desired) as well as short duration of sleep. Insomnia is frequently comorbid with depression and can also represent a risk factor for subsequent depression (5). Prevalence of insomnia symptoms may be as high as 75% among older adults. (6) Across studies, both subjectively reported insomnia and objectively measured sleep disruption (using polysomnography or wrist actigraphy) have been shown to predict worse depressive symptom ratings, higher rates of attrition in studies,

fluctuations in treatment response and suicidal ideation. Studies of sleep architecture indicate that major depressive disorder in late life is associated with changes (7), including lesser amount of time in slow wave sleep and a greater percentage of time spent in REM sleep, compared to non-depressed controls. Poor sleep can also impact functional ability. In one study, insomnia symptoms were found to be a risk factor for increased disability in tasks that may be related to higher levels of functioning and quality of life. The combination of insomnia and short sleep duration has also been associated with adverse physical health outcomes, including poor neurocognitive functioning, hypertension, diabetes, and mortality (6,8,10). Given the association between cardiovascular health and depression, sleep disruption may increase likelihood of negative physical outcomes associated with depression.

There is also important recent evidence (6) demonstrating the impact of sleep symptoms on depression treatment response. A study by Troxel and colleagues noted that sleep latency of 30 minutes or greater was associated with higher risk of non-remission of depression in response to both pharmacologic and non-pharmacologic approaches. Moreover, the presence of 3 or more sleep disturbances (e.g. insomnia, prolonged sleep latency, short duration of sleep, frequent awakenings) may triple the likelihood of non-remission.

The case of Mr. G. highlights how clinicians may be able to incorporate objective sleep measurement using wrist worn devices into regular clinical

care in an efficient, easy-to-use manner. The use of actigraphy has been recommended as a tool for identifying patient who may be at risk for poor depression outcomes because of poor sleep (6). While wrist-worn actigraphy may not be as accurate as polysomnography, several studies now utilize it as the primary objective measure of sleep. The current generation of wrist worn devices offer easily accessible and interpretable data that may simplify the process of regular clinical use of objective sleep measurement. Self-report has been noted to vary considerably from objectively measured sleep. In over 30% 0f the population, there may be variations of 1 hour or greater. Factors associated with higher variance include male gender, functional impairment and cognitive dysfunction (9).

In the case of Mr. G, there was a clinical dilemma posed by the discrepancy between his self-report and the collateral information provided by his wife. He fits the demographic profile most associated with unreliable self–reports of sleep (male gender, mild neurocognitive impairment), and because of his polypharmacy, the clinical implications of this discrepancy were amplified. Use of motion detecting technology facilitated that paient’s acceptance of the fact that eliminating two of his insomnia medications did not result in a significant change to his sleep patterns. This demonstrates how such technology may provide clinicians with data that fosters reduction of polypharmacy in older adults.

Psychomotor Retardation and Physical Activity in Depression

Depression in older adults, especially those with cognitive impairment can present primarily as amotivation and neurovegetative symptoms. (11). Psychomotor retardation has been reported as more common among older adults (12,13,14), and a syndrome of depression accompanied by executive dysfunction and characterized by such psychomotor retardation has been described (15). Apathy, which is a common syndrome in late life depression, can also include psychomotor retardation as a component (16).

This issue can create a diagnostic challenge for clinicians, since self-report of movement ability has been demonstrated as unreliable, especially if it is compounded by other conditions that impede movement, such as arthritis (17). Availability of objective tools to document and measure motion in real time may substantially improve clinicians' ability to establish the nature and extent of psychomotor retardation in older adults and can have impact on clinical decision making, as demonstrated in the case of Mr.G. With sensor technology proliferating and becoming increasingly ubiquitous, especially in smartphones, preliminary studies have suggested a role for such technology in monitoring mental health status (18). One study has demonstrated that motion-related data collected by cellphone sensors (including geospatial and kinesthetic activity) can correlate with changes in depression. Activity monitoring using wrist worn sensors in younger adults (19,20) have been shown in several studies as a reliable way of measuring movement changes in depression and the data collected are comparable to data collected from accelerometers worn on the trunk. Measuring movement of the trunk has

been historically considered the preferable way of capturing subtle changes in movement associated with mood, however, implementation of research-based actigraphy in regular clinical practice may not be feasible because of the additional time and effort that may be required to download and interpret these data, thus posing a significant barrier to adoption (21).

Movement, Exercise, Depression and Cognition

There is an extensive literature studying the impact of physical activity on the brain.

Though Mr. G was physically fit, his lack of motion may have played a role in the worsening of his physical health and has implications for his cognitive health as well. There have been extensive studies – both in animal models as well as humans – that document the impact of activity and especially aerobic exercise on the brain (22). Exercise has been demonstrated as having a molecular effect on the brain, including gene expression, neuroregeneration, synaptogenesis and vascularization that can improve and preserve cognition as well as enhance mood. The hippocampus and the frontal cortex may be especially sensitive to such changes. This is noteworthy because these regions of the brain are susceptible to the fastest rates of atrophy in late life (1-2% per year) and cognitive dysfunction may accelerate this rate of degeneration (23). The possibility that better overall fitness and regular exercise can help slow this rate of atrophy offers an intriguing therapeutic target. It is also noteworthy that cognitive training, which has received great

attention in the media, does not appear to have an impact on rates of age-related atrophy in any brain region (23). These studies point towards the possibility that monitoring and improving physical activity may have greater benefits on cognitive function that the vast array of brain training games and applications that are available commercially and are being heavily marketed.

There is a vast and well-characterized literature documenting the beneficial effects of physical exercise, especially aerobic exercise, on depression. A recent Cochrane Meta analysis noted that pooled data from 37 clinical trials indicated a modest beneficial effect of exercise over placebo in reducing depressive symptoms. (24) (Standardized Mean Difference (SMD = -0.62), When the authors narrowed the search to only studies that reported long term effects of exercise, the effect persisted, though it shrank (SMD = -0.33). Studies indicated that the efficacy rates for exercise were comparable to pharmacotherapy and psychotherapy, with possibly higher rates of adherence. While it remains unclear what types of exercise, what durations, and what sorts of settings (indoor vs. outdoor) may be optimal, this meta-analysis indicates that resistance training and mixed exercise may be more beneficial than just aerobic exercise, and that a higher number of sessions may be more beneficial.

As we note above, subsyndromal depression (SSD) may be three times more prevalent than major depression and may not respond to medications (4). Physical activity has been demonstrated as efficacious in managing these symptoms (3)

For clinicians, these data provide direction on how to discuss physical activity with their patients. Technology can also serve a key role in facilitating better physical activity. For example, use of commercially available “exergames,” or video games that involve physical activity have been demonstrated as significantly improving SSD in older adults (25). Using such technology can help improve intrinsic motivation to engage in physical activity and wrist-worn monitors can help physicians track adherence.

Using motion-sensing technology with Mr. G. allowed for the improvement in his degree of activity to be visualized. This had a dual benefit: 1) the ability to track improvement in psychomotor retardation as the medication changes took effect and 2) a rationale for him to increase the length and duration of his daily walks once he felt less depressed. This added a therapeutic factor that may have augmented the antidepressant effect of exercise.

Technology adoption by older adults:

The easier technology is to use, and the easier it is to visualize data, the more likely that physicians and patients will adopt it. Simultaneously, older adults are likely to adopt technology only if it performs a function that they cannot currently perform and that use of this technology is likely to lead to tangible benefit, while being easy to use (26).

The current generation of commercially available wrist-worn fitness monitors and smart watches include built-in sophisticated three-dimensional accelerometers and software that can seamlessly process and present easily

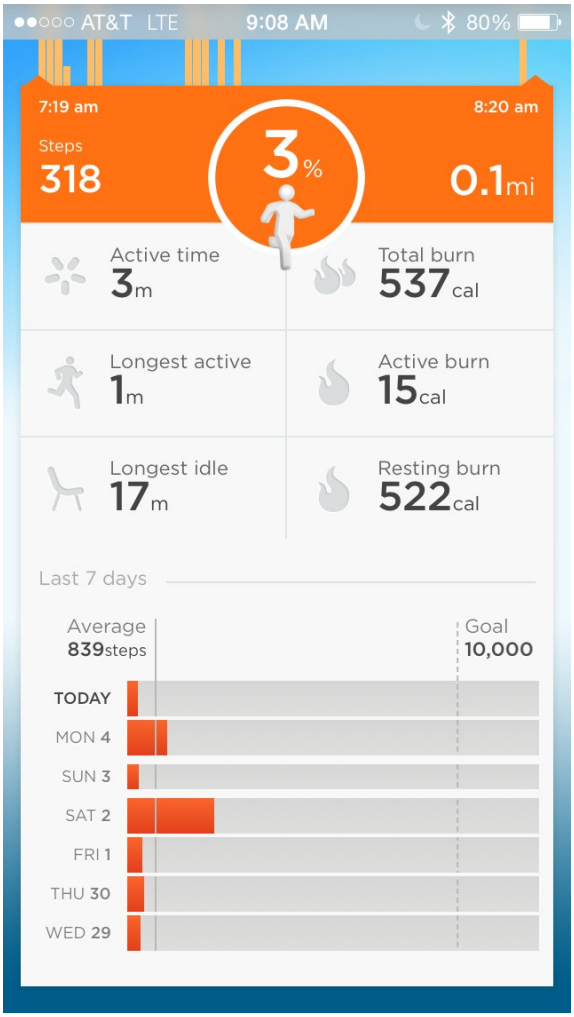
visualized data. Moreover, about 25% of adults over 55 already own a fitness monitor, suggesting that transitioning these devices for clinical application may be simpler for clinicians than teaching older adults brand new technology with which they may not be familiar. This is likely to increase the odds of adherence. (27). While much of the effort of the health technology industry has been on developing devices targeted at specific health problems and specific demographics, our experience with Mr. G suggests an alternate approach by clinicians may have a greater payoff. Widely available, popular technologies may be more acceptable to patients, may often be cheaper, and with clear direction and application, can help clinicians add a dimension to care that was previously not possible.

Summary

The case of Mr. G highlights several important points. This case demonstrates the feasibility of utilizing motion-sensing technology in a clinical environment with older adults who have comorbid mood and cognitive symptoms. It also demonstrates that use of such technology can add a dimension to clinical diagnostics that was not previously readily available. While there are limitations to using commercially available wrist-worn devices for monitoring motion and sleep in older adults, including the fact these may not be as accurate as polysomnography (28,29), and that information on the steps taken still needs validation and context based on observational data, this case report provides context for how these devices

may add a dimension to clinical care, as a result of maturation of the technology involved and availability of immediately visible processed data. With further development, such data may even serve as biomarkers of response to antidepressant treatment and guide personalized care (30). Future work should assess clinician attitudes and concerns about using commercially available devices for psychiatric care. Future engineering projects should focus on how more nuanced information on movement and behavior may be captured in a non-invasive manner from persons with psychiatric diagnoses.

Figure 1: Image of patient's cellphone, indicating psychomotor retardation



References:

1) Wang S, Blazer DG. Depression and cognition in the elderly. Annu Rev Clin Psychol. 2015;11:331-60
2) Blazer D. Depression in late life: review and commentary. J. Gerontol. A Biol. Sci. Med. Sci. 2003; 58(3):249–65
3) Meeks TW, Vahia IV, Lavretsky H, Kulkarni G, Jeste DV. A tune in "a minor" can "b major": a review of epidemiology, illness course, and public health implications of subthreshold depression in older adults. J Affect Disord 2011; Mar;129(1-3):126-42
4) Vahia IV, Meeks TW, Thompson WK, Depp CA, Zisook S, Allison M, Judd LL, Jeste DV. Subthreshold depression and successful aging in older women. Am J Geriatr Psychiatry. 2010 Mar;18(3):212-20
5) Spira AP, Kaufmann CN, Kasper JD, Ohayon MM, Rebok GW, Skidmore E, Parisi JM, Reynolds CF 3rd. Association between insomnia symptoms

and functional status in U.S. older adults. J Gerontol B Psychol Sci Soc Sci. 2014 Nov; 69 Suppl 1:S35-41.

6) Troxel WM, Kupfer DJ, Reynolds CF 3rd, Frank E, Thase ME, Miewald JM, Buysse DJ. Insomnia and objectively measured sleep disturbances predict treatment outcome in depressed patients treated with psychotherapy or psychotherapy-pharmacotherapy combinations. J Clin Psychiatry. 2012 Apr;73(4):478-85.

7) Smagula SF, Reynolds CF 3rd, Ancoli-Israel S, Barrett-Connor E, Dam TT, Hughes-Austin JM, Paudel M, Redline S, Stone KL, Cauley JA; for the Osteoporotic Fractures in Men (MrOS) Research Group. Sleep Architecture and Mental Health Among Community-Dwelling Older Men. J Gerontol B Psychol Sci Soc Sci. 2013 Dec 10. [Epub ahead of print]

8) Vgontzas AN, Liao D, Pejovic S, Calhoun S, Karataraki M, Bixler EO. Insomnia with objective short sleep duration is associated with type 2 diabetes: A population-based study. Diabetes Care. 2009 Nov;32(11):1980-5.

9) Van Den Berg JF[1], Van Rooij FJ, Vos H, Tulen JH, Hofman A, Miedema HM, Neven AK, Tiemeier H. Disagreement between subjective and actigraphic measures of sleep duration in a population-based study of elderly persons. J Sleep Res. 2008 Sep;17(3):295-302

10) Fernandez-Mendoza J, Calhoun S, Bixler EO, Pejovic S, Karataraki M, Liao D, Vela-Bueno A, Ramos-Platon MJ, Sauder KA, Vgontzas AN Insomnia with objective short sleep duration is associated with deficits in neuropsychological performance: a general population study. Sleep 2010 Apr; 33(4): 459-65

11) Li Y, Meyer JS, Thornby J. Depressive symptoms among cognitively normal versus cognitively impaired elderly subjects.Int J Geriatr Psychiatry. 2001 May;16(5):455-61.

12) Beheydt LL, Schrijvers D, Docx L, Bouckaert F, Hulstijn W, Sabbe B. Psychomotor retardation in elderly untreated depressed patients. Frontiers in Psychiatry. 2015 Jan 26;5:196

13) Kertzman S, Reznik I, Hornik-Lurie T, Weizman A, Kotler M, Amital D. Stroop performance in major depression: selective attention impairment or psychomotor slowness? J Affect Disord. 2010 Apr;122(1-2):167-73.

14) Cheng H, Gurland BJ, Maurer MS. Self-reported lack of energy (anergia) among elders in a multiethnic community. J Gerontol A Biol Sci Med Sci. 2008 Jul;63(7):707-14.

15) Alexopoulos GS, Borson S, Cuthbert BN, Devanand DP, Mulsant BH, Olin JT, Oslin DW. Assessment of late life depression. Biol Psychiatry. 2002 Aug 1;52(3):164-74.

16) Yuen GS, Bhutani S, Lucas BJ, Gunning FM, AbdelMalak B, Seirup JK, Klimstra SA, Alexopoulos GS. Apathy in late-life depression: common, persistent, and disabling. Am J Geriatr Psychiatry. 2015 May;23(5):488-94

17) Kriegsman DM, Deeg DJ, van Eijk JT, Penninx BW, Boeke AJ. Do disease specific characteristics add to the explanation of mobility limitations in patients with different chronic diseases? A study in The Netherlands. J Epidemiol Community Health. 1997 Dec;51(6):676-85.

18) Ben-Zeev D, Scherer EA, Wang R, Xie H, Campbell AT. Next-Generation Psychiatric Assessment: Using Smartphone Sensors to Monitor Behavior and Mental Health. Psychiatr Rehabil J. 2015 Apr 6. [Epub ahead of print]

19) Burton C, McKinstry B, Szentagotai Tătar A, Serrano-Blanco A, Pagliari C, Wolters M Activity monitoring in patients with depression: a systematic review. J Affect Disord. 2013 Feb 15; 145(1):21-8.

20) Reichert M, Lutz A, Deuschle M, Gilles M, Hill H, Limberger MF, Ebner-Priemer UW. Improving motor activity assessment in depression: which sensor placement, analytic strategy and diurnal time frame are most powerful in distinguishing patients from controls and monitoring treatment effects. PLoS One. 2015 Apr 17;10(4)

21) Schneider T, Panzera AD, Martinasek M, McDermott R, Couluris M, Lindenberger J, Bryant C. Physicians' perceptions of mobile technology for enhancing asthma care for youth. J Child Health Care. 2014 Nov 26.[Epub ahead of print]

22) Erickson KI, Gildengers AG, Butters MA. Physical activity and brain plasticity in late adulthood. Dialogues Clin Neurosci. 2013 Mar;15(1):99-108.

23) Raz N, Schmiedek F, Rodrigue KM, Kennedy KM, Lindenberger U, Lövdén M.
Differential brain shrinkage over 6 months shows limited association with cognitive practice. Brain Cogn. 2013 Jul;82(2):171-80.

24) Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, McMurdo M, Mead GE. Exercise for depression. Cochrane Database Syst Rev. 2013 Sep 12;9

25) Rosenberg D, Depp CA, Vahia IV, Reichstadt J, Palmer BW, Kerr J, Norman G, Jeste DV. Exergames for subsyndromal depression in older adults: a pilot study of a novel intervention. Am J Geriatr Psychiatry. 2010 Mar;18(3):221-6.

26) Davenport RD, Man n W, Lutz B. How older adults make decisions regarding smart technology: an ethnographic approach. Assist Technol. 2012 Fall; 24(3):168-81

27) https://www.npd.com/wps/portal/npd/us/news/press-releases/2015/the-demographic-divide-fitness-

trackers-and-smartwatches-attracting-very-different-segments-of-the-market-according-to-the-npd-group/
28) Ancoli-Israel S1, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. Sleep. 2003 May 1;26(3):342-92.
29) Ray MA, Youngstedt SD, Zhang H, Robb SW, Harmon BE, Jean-Louis G, Cai B, Hurley TG, Hébert JR, Bogan RK, Burch JB Examination of wrist and hip actigraphy using a novel sleep estimation procedure; Sleep Sci. 2014 Jun;7(2):74-81.
30) Alexopoulos GS. Personalizing the care of geriatric depression. Am J Psychiatry. 2008 Jul;165(7):790-2