Activity monitoring in patients with depression: a systematic review.

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Word count 3316

Abstract

Background

Altered physical activity is an important feature of depression. It is manifested in psychomotor retardation, agitation and withdrawal from engagement in normal activities. Modern devices for activity monitoring (actigraphs) make it possible to monitor physical activity unobtrusively but the validity of actigraphy as an indicator of mood state is uncertain. We carried out a systematic review of digital actigraphy in patients with depression to investigate the associations between measured physical activity and depression.

Methods

Systematic review and meta-analysis. Studies were identified from Medline, EMBASE and Psycinfo databases and included if they were either case control or longitudinal studies of actigraphy in adults aged between 18 and 65 diagnosed with a depressive disorder. Outcomes were daytime and night-time activity and actigraphic measures of sleep.

Results

We identified 19 eligible papers from 16 studies (412 patients). Case control studies showed less daytime activity in patients with depression (standardised mean difference -0.76, 95% confidence intervals -1.05 to -0.47). Longitudinal studies showed moderate increase in daytime activity (0.53, 0.20 to 0.87) and a reduction in night-time activity (-0.36, -0.65 to -0.06) over the course of treatment.

Limitations

All study participants were unblinded. Only 7 papers included patients treated in the community.

Conclusions

Actigraphy is a potentially valuable source of additional information about patients with depression. However, there are no clear guidelines for use of actigraphy in studies of patients with depression. Further studies should investigate patients treated in the community. Additional work to develop algorithms for differentiating behaviour patterns is also needed.

KEYWORDS: Depressive disorder; actigraphy; telemonitoring.

Background

Altered physical activity has long been recognised as a feature of depression (Parker and Brotchie, 1992). Psychomotor retardation is argued to be a cardinal feature of melancholia (Parker et al., 1995) but other forms of altered physical activity in depression include agitation and withdrawal from normal activities of daily living. Reports of activity, either observed or self reported, are features of many validated depression assessment tools (Hamilton, 1960; Kroenke et al., 2001).

Objective measurement of activity (actigraphy) using body-worn accelerometers has been available in research settings for over 20 years and accelerometers have been used extensively in research in a wide range of situations to measure both daytime activity (Matthews et al., 2012) and sleep (Martin and Hakim, 2011). In recent years devices incorporating these technologies have become widely available, and - in the case of smartphones – ubiquitous. Much of their use is currently driven by the health and lifestyle market. While research and commercial applications are beginning to use activity monitoring in patients with depression (Help4Mood Consortium, 2012;ICT4 Depression Consortium, 2012;Monarca Project, 2012;Optimi Consortium, 2012), we were unable to find a recent systematic review of the extent to which actigraphic measures of activity correspond to clinically meaningful changes in depression. We were also unable to find any guidelines for the use of activity monitoring in depression in order to recommend, for instance, how long patients should wear the actigraphy device or what is the best way of characterising activity patterns during the measurement period.

We carried out a systematic review of published studies in which actigraphy was used to monitor day or night time activity in people with a depressive disorder. We included both case-control studies which examined the difference between people with depression and healthy controls and longitudinal (pre-post) treatment studies to investigate changes over time. The review had two aims:

(1) to examine the association between activity levels and depression

(2) to identify areas of research that need to be addressed before guidelines for the use of actigraphy in people with depression can be developed

Methods

The study was conducted in accordance with PRISMA statement (Moher et al 2009) and the protocol was agreed by all authors in advance of data collection. As the study included no direct involvement with patients or identifiable data no ethical review was necessary.

Eligibility

We included case-control and longitudinal treatment studies of adults aged between 18 and 65 which used actigraphy. At least one group in the study was required to have a confirmed diagnosis of major depressive disorder, depression in association with bipolar disorder, or Seasonal Affective Disorder (SAD) during the winter season. Eligible studies could include participants treated in hospital or at home.

Search Strategy

We searched Medline, PsychInfo and EMBASE databases for publications between 1966 and April 2012 which included the MESH heading depression/ and one or more of the eight terms monitoring, ambulatory/, motor activity/, actigrap$ or actimet$ or actograp$, actomet$ or accelerometer. We also followed references from retrieved publications and searched Google Scholar for relevant grey literature.

Study Selection

After removal of duplicates, two authors (CB and MW) reviewed the titles of all publications identified by the searches to identify potentially eligible abstracts. The same two authors independently and then jointly selected studies for detailed extraction based on the full abstract. Studies were eligble if they included appropriate data from adults aged 18-65 with a diagnosis of depression. Studies were excluded if they included only patients with bipolar disorder, or were limited to patients with potentially confounding conditions - mostly cancer. Where two or more publications appeared to relate to the same data, we included both provided they reported on separate measures (for instance sleep in one and daytime activity in another). For each included study two authors (CB plus either AS, ASB, BM or MW) independently extracted data onto a form that had been developed by CB for this review. The data comprised study design and location; characteristics of the sample (patient and where relevant control), actigraphic monitoring parameters (duration of monitoring, quantifications of activity) and relevant outcomes.

As part of the data extraction, studies were assessed for risk of bias in relation to patient recruitment, blinding of analysis, potential confounders, multiple publication, and

reporting bias (such as failure to report hypotheses which were tested and over-reliance on post-hoc analysis). Any discrepancies were corrected by referring to original studies and resolved by consensus.

Choice of outcomes

In advance of data extraction, we specified two primary outcomes: day-time activity and night-time activity (each recorded as total or average counts for all, or a substantial portion of, the relevant time period). We aimed to examined these separately in case-control and longitudinal studies. In addition, after reading the eligible papers, we included four additional outcomes: sleep efficiency, sleep duration, and two measures of diurnal variation – intra-day variability, i.e., variation in activity levels within one day, and inter-day stability, i.e., variation in activity levels from day to day.

Data analysis

From each study we extracted data on daytime and night time activity as available. Where studies reported total (or average) daytime activity we used this; where studies chose other time periods, such as total 24 hour activity or most active 10 hours we extracted these. From each set of data we calculated a measure of the difference between groups (either case-control or pre-post treatment) using the standardized mean difference. We made forest plots of all comparisons and assessed heterogeneity between studies. Heterogeneity was reported as the I^2 statistic, where higher values indicate greater heterogeneity and values of over 50% may indicate substantial heterogeneity (Higgins and Green 2011). Where heterogeneity was less than 50% we carried out meta-analysis using a random effects model because of the variety within study populations with respect to severity, location and treatment.

Results

Search results

The initial search returned 1267 titles. From these and subsequent following of references, we reviewed 81 abstracts and obtained full texts for 24 publications from 20 studies. In addition data from two papers which were no longer available (Foster et al., 1978; 9) were extracted from an earlier review (Teicher, 1995) resulting in a total of 26 papers for data extraction. This is summarised in Figure 1. Following data extraction 8 papers were excluded: 3 for having no interpretable data (Iverson, 2004; Ueda et al., 2005; Wolff, III et al., 1985), two conference abstracts with insufficient data (Deoras et al., 2010; Kelly et al., 2009), two for inappropriate comparisons (Lemke et al., 1998; Mendlowicz et al., 1999) and one as an exploratory study of non-linear dynamic measures of variability (Hauge et al., 2011). This left 19 papers from 16 studies suitable for detailed comparison(Baune et al 2006; Baune et al 2007; Berle et al., 2010; Coffield and Tryon, 2004; Faurholt-Jepsen et al., 2012; Foster et al., 1978; Glod et al 1992; Godfrey and Knight, 1984; Haynes et al., 2006; Joffe et al., 2009;Korszun et al., 2002; Raoux, 1994; Royant-Parola et al., 1986; Teicher et al., 1997; Todder et al., 2006; Todder et al., 2007; Volkers et al., 2002; Volkers et al., 2003; Winkler et al., 2005)

Study characteristics

Relevant study characteristics are summarized in Table 1 which also includes a reference number for each study. Eleven publications were from Europe (4 from Germany, 2 from the Netherlands and one each from Austria, Denmark, France, Norway and UK), 7 from the USA and 1 from New Zealand. Thirteen papers reported

on hospital inpatients, 7 reported data from outpatients or primary care patients (one paper included both).

Of the 19 papers, eight included patients with major depression in association with bipolar disorder, five with type II only (1-4;10) and three with both type I and type II (5;14;15). One included a separate group of patients with bipolar disorder – these were not included in the analysis. Three papers examined depression in patients with Seasonal Affective Disorder (9;16;19). The diagnosis of major depressive disorder was confirmed using a standardised interview in 13 papers; most of those without structured interview inclusion took place before 1995.

Most study populations had a greater proportion of female than male participants (median 57, interquartile range 43 to 80). Studies had a broadly similar average participant age, (median 44, interquartile range 38 to 50 years). Antidepressant drug treatment was prescribed in 11 studies (1-5; 8;11;13-15;17), and stated to be not prescribed in 4 (of which 3 were studies of seasonal affective disorder) (9;16;18;19). Antidepressant prescribing was not reported in 3 papers (6;10;12). The antidepressant drugs prescribed varied within and between studies, generally using conventional treatment at the time the study was conducted, one study allocated patients to either a tricyclic antidepressant or selective serotonin reuptake inhibitor (SSRI) (17). An atypical antipsychotic (quetiapine) was routinely prescribed in 5 papers (1-5).

Study design, risk of bias and confounding

Eleven papers reported a case control design (4;5; 8-13;16;18;19) and 10 reported before and after treatment comparisons for patients (1-4;6;10;14;15;17;19), of which 3 papers reported also data from healthy controls (10;4;19).

All papers reported either day time or sleep actigraphy data and 7 of the 15 studies (11 papers) reported both daytime and sleep data. While all studies used wrist actigraphy, they varied substantially in the activity measures reported and these are summarized in table 2. Because studies used a range of devices and differed in reporting periods (some reporting totals, others hourly averages) the reports of activity counts could not be directly compared between studies; however the use of standardized mean difference for comparisons allowed these to be combined in the meta-analysis (Higgins and Green 2011).

Most studies contained significant risk of bias: all were observational studies in which participants were aware of their allocation group and of being recorded. Therefore, they may have altered behaviour accordingly. Most studies appeared to use opportunistic recruitment strategies such as available in-patients rather than systematic selection and few gave details of how many patients were considered but not eligible. Three studies carried out before 1995 failed to describe blinding of data analysts. We regarded studies of depressed hospital inpatients compared to community dwelling healthy controls as at high risk of confounding and thus having low external validity. Almost all studies were at some risk of confounding due to the effects of depression treatments and there was insufficient data to quantify this. Duplication bias was considered in a group of papers

which appeared to come from the same study although three of the four reported different data (1-4).

Daytime activity

Daytime activity was reported in 15 papers (1;2;4;5;7-10; 13-19). Of these, 10 compared data from cases and controls (4;5;7-10;13;16;18;19) and 8 made pre and post treatment comparisons (1;2;4;10;14;15;17;19). Eleven papers included hospital in-patients (1;2;4; 5; 8-10;14;15;17;18) and 4 papers included outpatients (5;7;13;16;19). Duration of monitoring varied between 3 and 30 days.

Eight case control studies including 208 cases and 245 controls had sufficient data for quantitative comparison (5;7; 8;9;13;16;4;18;19). One included study reported the median value for both groups (7); the median was used in comparisons with the standard deviation calculated from the interquartile range. One study did not report the standard deviation data for controls and was excluded from the comparison (10). Meta-analysis showed moderate heterogeneity between studies (I^2= 47.5) and the results are shown in figure 2a. There was a significant difference in standardized mean daytime activity between cases and controls of -0.76 (-1.05 to -0.47); this was similar in studies involving inpatients (-0.8) and those conducted in outpatients (-0.72).

Seven pre and post treatment studies, including 163 patients had sufficient data for quantitative comparison (2;4;10;14;15;17;19). Of these studies, 6 were conducted with hospital inpatients. Figure 2b shows the forest plot of the meta-analysis. There was moderate heterogeneity between studies (I^2= 48.4). There was a significant increase in standardized mean daytime activity following treatment of 0.53 (0.2 to 0.87).

Sleep and night-time activity

Fourteen papers reported night time activity (1;3-6;8;9;11-14;17-19). Of these, 9 compared data from cases and controls (4;5; 8;9;11-13;18;19) and 7 made pre and post treatment comparisons (1;3;4;6;14;17;19). Ten papers included hospital in-patients (1; 3-5;6;8;9;14;17;18) and 5 papers included outpatients (5; 11-13;19). Duration of monitoring varied between 2 and 14 nights.

Night time actigraphic activity was reported in 6 case control studies, including 146 cases and 179 controls with data suitable for quantitative comparison (4;5;8;9;13;18). All studies used in-patient cases compared to healthy controls living at home. Figure 2c shows the forest plot of the comparison. There was substantial heterogeneity between studies (I^2= 88.9) and in view of this we made no estimate of an overall effect.

Night time activity was also reported in 3 pre and post treatment studies, including 89 patients (1; 4;17). All 3 of these studies were conducted in hospital inpatients. Figure 2d shows the forest plot of the meta-analysis. There was low heterogeneity between studies (I^2= 0) and meta-analysis showed a small reduction in mean overnight activity following treatment -0.36 (-0.65 to -0.06).

Sleep efficiency before and after treatment was reported in 2 studies (3; 19) and sleep duration in 3 (14; 3; 19). Effects appeared to be small, with pooled SMD of 0.19 (-0.38 to 0.76) and -0.1 (-0.44 to 0.23) respectively.

Variability

Two measures, inter-day stability and intra-day variability were reported before and after treatment in 2 studies (1; 5) including only 33 patients. There was no evidence of a meaningful difference, with pooled SMD of 0.15 (-0.35 to 0.65) and 0.04 (-0.44 to 0.52) respectively.

Discussion

Summary of principal findings

Actigraphy confirms the clinical impression that patients with depression display less day-time motor activity than healthy controls and that this activity increases over the course of treatment. Depressed patients appear to have increased night-time activity although this is not apparent in standard actigraphic measures of sleep duration or sleep efficiency. Studies to date have used a wide range of protocols and most have been confined to hospital inpatients.

Strengths and limitations

This is the first review of actigraphy in patients with depression to take a systematic approach to literature searching and synthesis. Searching and data extraction were both carried out in parallel by two investigators, with discrepancies resolved by discussion.

The principal limitation is the problem of combining such disparate studies. We considered whether, given the heterogeneity of depression, treatment and contexts, this was appropriate. We took the view that altered activity patterns may be present across a wide range of depressive disorders and as long as studies had suitably rigorous methods, then it would be appropriate to combine them, at least qualitatively. While the subgroup of studies including patients with SAD was too small for formal comparison

with other studies, qualitative inspection of the results suggests they were comparable with those of patients with non-seasonal depression. We included studies which in which the depressed patients included some with bipolar disorder. One study examined three groups: unipolar, bipolar and healthy controls and found a difference between depression types but there were insufficient data within other studies to examine this.

We examined all studies systematically for sources of bias. The main problem we identified was with confounding – particularly in studies comparing depressed inpatients with healthy controls living in the community. Not surprisingly these studies showed large differences between groups which could have been accounted for by living environment and routines rather than by depression. In contrast, the longitudinal treatment studies were more robust to this form of confounding. We did not attempt to separate out drug treatment effects, firstly because in most studies patients received a mix of treatments and secondly because the agents in use changed repeatedly over the period from the first to the last of these studies.

While the actigraphy devices in all the studies used the same principle of movement detection with a device containing an accelerometer attached to the patient's wrist, not all studies mentioned the make and model of actigraph used. The most commonly used models were the MotionloggerTM Actigraph (Ambulatory Monitoring, Inc, Ardsley, NY) and the Actiwatch (Cambridge Neurotechnology Ltd, UK). None of the studies used waist actigraphy, which is a well-established method for data on daytime activity levels and exercise (Troiano et al., 2008). None of the sleep studies used polysomnography which is the gold standard for sleep assessment, although correlation of this with actigraphy appears to be good (McCall and McCall, 2012).

There was considerable variation in the duration of sampling ranging from twelve hours to more than two weeks. All but one study included data collection periods of at least 3 days, as recommended in a review of actigraphy methods in cancer studies (Berger et al., 2008) although this may not be sufficient to minimise the influence of day to day variation (Baranowski et al., 2008). There was inconsistent reporting of depression severity, medication or other variables which may influence activity such as body mass index. In order to examine the influence of these factors would have required an individual patient meta-analysis which was outside the scope of this study.

Interpretation

Taken together, these studies provide good evidence of differences in the daytime activity of hospitalised patients with depression both compared to controls and over time. However, generalisability to people with depression living in the community is problematic. Most of the studies of outpatients examined patients with SAD or specific subgroups such as menopausal women; only one small study investigated daytime activity in non-seasonal depression (13). Most patients treated in the community will have milder forms of depression and less co-morbidity than those admitted to hospital and it is not clear from data in these studies whether changes in activity are limited to patients with more severe or melancholic depression. In future it may be that more sophisticated interpretation of actigraphy may be able to discriminate psychomotor retardation, agitation and normal activity.

Implications for research, policy and practice

Actigraphy is a prominent feature of innovative telehealth approaches for monitoring the long-term health and recovery of people with depression (Help4Mood Consortium, 2012;ICT4 Depression Consortium, 2012;Monarca Project, 2012;Optimi Consortium, 2012). However, the results of this review suggest six issues that need to be addressed in order to ensure that activity monitoring is worthwhile:

(1) Further evidence is needed to inform clinical guidelines for the use of actigraphy in the monitoring and management of depression, as has been proposed for patients with cancer (Berger et al., 2008). These should take account of different patient populations (e.g. acute versus chronic cases) and settings (e.g. community versus hospital).

(2) Field studies are needed in order to determine to what extent the activity levels of people with depression living in the community differ from existing population norms (Troiano et al., 2008)

(3) Longitudinal data is needed on the correlation of actigraphy data in people living in the community with other validated measures used to assess recovery.

(4) Very little is known about the acceptability of different actigraphy devices and protocols to people with depression. Such information is crucial for ensuring adherence to monitoring. While almost all the studies reported here used a wrist-worn device, chest worn combined monitors may increase acceptability in addition to collecting additional data (Brage et al 2005).

(5) Analytical methods need to be improved to ensure all relevant features are extracted from actigraphy data (Hauge et al., 2011) (Nakamura et al., 2008). Methods need to be developed to categorise different behaviour types (Matthews et al., 2012) and standardised in order to capture any differences in the diurnal variation of activity.

(6) In view of the recent demonstration of differences in activity between patients with unipolar and bipolar depression (Faurholt-Jepsen et al 2012), further studies should characterise actigraphic differences between these two disorders.

Collaboration between academic experts, clinicians and healthcare data custodians will be important in order to make best use of these new data streams for patient care and research.

Conclusions

Actigraphy is a potentially valuable source of additional information in patients with depression. Guidelines for use of actigraphy in studies of patients with depression are needed and further studies should investigate patients treated in the community and create analysis methods for differentiating relevant behaviour patterns.

Figure 1 Flowchart indicating number of eligible studies.

(see separate png file)

Figure 2 - Forest plots of systematic review of actigraphy using different study types and outcomes.

(see separate png file)

Table 1: Characteristics of study patient populations

Study	ID	Paper	Country	Diagnosis[1]	Bipolar	Age	% female	Scale[2]	Interview	Drugs[3]	Notes
Baune	1	Baune et al 2006	Germany	MDD	Type II	48 (16)	80	B,H	SCID	AD,AP	2/10 Bipolar II
	2	Baune et al 2007	Germany	MDD	Type II	49 (13)	48	B,H	SCID	AD,AP	Treatment Resistant Depression, 6/27 BipolarII
	3	Todder et al 2006	Germany	MDD	Type II	49 (13)	48	B,H	SCID	AD,AP	as Baune 2007
	4	Todder et al 2009	Germany	MDD	Type II	49 (13)	48	B,H	SCID	AD,AP	as Baune 2007
Berle	5	Berle et al 2010	Norway	MDD	Type I & II	43 (11)	56	M	"standard"	AD,AP	7/23 Bipolar II; 1/27 Bipolar I
Coffield	6	Coffield & Tyron 2004	USA	MDD	No	30 (12)	39	B	"Clinical"	NS	
Faurholt-Jepsen	7	Faurholt-Jepsen et al 2012	Denmark	MDD	No	38 (12)	69	H	SCID	AD	Study tested Unipolar vs Bipolar vs Controls. Data from bipolar not shown
Foster	8	Foster et al 1978	USA	MDD	No	25 (5)	57	None	ns	AD	
Glod	9	Glod et al 1992	USA	SAD	No	38 (13)	81	None	ns	None	
Godfrey	10	Godfrey & Knight 1984	NZ	MDD	Type II	na	na	Other	"standard"	NS	
Haynes	11	Haynes et al 2006	USA	MDD	No	44 (13)	31	H	SCID	AD	n=41 of the sample were veterans; uneven medication status,
Joffe	12	Joffe et al 2009	USA	MDD	No	51 (5)	100	B	SCID	NS	All menopausal, 70% MDD; 17% Dysthymia; 13% minor dep
Korszun	13	Korszun et al 2002	USA	MDD	No	46 (3)	55	None	SCID	AD	two additional groups, fibromyalgia +- depression excluded from analysis.
Raoux	14	Raoux 1994	France	MDD	Type I & II	44 (21)	78	M	"Clinical"	AD	5/26 Bipolar

[1] MDD; Major Depressive Disorder; SAD: Seasonal Affective Disorder.
[2] B: Beck Depression Inventory; H: Hamilton Depression Rating Scale; M: Montgomery Asberg Depression Rating Scale
[3] AD: Antidepressant; AP: Antipsychotic (typically Quetiapine XL)

Royant Parola	15	Royant Parola et al 1986	UK	MDD	Type I & II	55 (na)	83	H,M	"Clinical"	AD	
Teicher	16	Teicher et al 1997	USA	SAD	No	39 (11)	80	None	SCID	None	
Volker 02	17	Volker et al 2002	NL	MDD	No	53 (9)	32	H	SCID	AD	Patients randomised imipramine vs. fluvoxamine
Volker 03	18	Volker et al 2003	NL	MDD	No	53 (9)	44	H	SCID	None	
Winkler	19	Winkler et al 2005	Austria	SAD	No	37 (14)	76	H	SCID (seasonal)	None	recruit by advert

Table 2: Study designs and actigraphy details

	Study Design			Number of participants		Actigraphy Details			
Paper	Period	Design[1]	Treatment	Case /Pre	Control / Post	Position	Duration (days)	Interval	Sleep diary
Baune 2006	Day	PP	Inpatient	10	10	Wrist	7	14	y
Baune 2007	Day	PP	Inpatient	27	27	Wrist	11	11	y
Todder 2006	Sleep	PP	Inpatient	27	27	Wrist	7	14	y
Todder 2009	Both	Both	Inpatient	27	27	Wrist	7	14	y
Berle 2010	Day	CC	Both	23	23	Wrist	14		n
Coffield 2004	Sleep	PP	Inpatient	18	21	Wrist	7	28	y
Faurholt-Jepsen 2012	Both	CC	Outpatient	20	31	Chest	3		n
Foster 1978	Day	CC	Inpatient	7	7	Wrist	na		n
Glod 1992	Day	CC	ns	26	21	Wrist	na		n
Godfrey 1984	Day	PP	Inpatient	5	9	Wrist	15	continuous	n
Haynes 2006	Sleep	CC	Outpatient	39	39	Wrist	5		y
Joffe 2009	Sleep	CC	Outpatient	52	51	Wrist	2		y
Korszun 2002	Day	CC	Outpatient	9	28	Wrist	6		y
Raoux 1994	Both	PP	Inpatient	26	26	Wrist	3	20	y
Royant Parola 1986	Day	PP	Inpatient	12	12	Wrist	30	30	y
Teicher 1997	Day	CC	Outpatient	25	20	Wrist	3		n
Volker 2002	Both	PP	Inpatient	52	52	Wrist	3	28	n
Volker 2003	Day	CC	Inpatient	54	64	Wrist	3		y
Winkler 2005	Both	Both	Both	17	17	Wrist	7	21	y

1 CC: Case-control design; PP: Pre- post treatment design

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